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Edited by

LEWIS STEPHEN PILCHER, M.D., LL.D., of New York

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ANNALS *of* SURGERY

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A HISTORY OF THYROID SURGERY*

By Casper F. Hegner, M.D.

of Denver, Colo.

From the beginning, fatalities attendant upon injuries to the neck emphasized this region as the most vulnerable in the human body. Lesions here are conspicuous. It is only natural that these, especially enlargements of the thyroid gland, should have attracted early medical attention.

In the time of Celsus,[1] the thyroid gland as a normal structure was not recognized. Enlargements called goüetre or hernia guttures were considered independent new formations, either parenchymatous or cystic in character.

In communities where goitre was endemic it was considered an inoperable and frequently fatal affliction. Death was commonly the result of respiratory obstruction. Surgical relief was invoked for disfigurement, dyspnœa or dysphagia.

No other condition has attracted more attention or has been given more careful study than diseases of the thyroid gland. Little of primary importance has been discovered as to the cause, and nothing really new has been added to the therapy of goitre in the past forty years. A better understanding of the rôle played by iodine, whose beneficial effects have been known for more than a hundred years, and which has been used as a prophylactic and therapeutic remedy for nearly that long, thanks to Plummer, is now more rationally and widely used.[2]

Moritz Schiff, a physiologist of Geneva, in 1856, showed by experiments on dogs that total extirpation of the thyroid gland produced a sequence of ill effects which led to death. His work was overlooked for more than twenty-five years. Neither Sick, Reverdin nor Kocher made reference to Schiff when they first reported the phenomena of surgical thyroid deprivation.

Schiff, in 1884, demonstrated the symptoms of thyroid deprivation could be averted by making thyroid transplants before performing complete extirpation of the gland. He proved the thyroid gland had a secretion which is necessary to life. He paved the way for the administration of thyroid extract in the treatment of myxœdema which was introduced in 1891 by Murray and Howitz.[3]

Frederich Von Müller, in 1893, demonstrated an increased metabolism in exophthalmic goitre.[4] His work led to the study of metabolism in all forms of goitre. The basal metabolic rate has become a cardinal index of the physiological status of the thyroid gland. It is an essential diagnostic and prognostic criterion.

Eugen Bauman, in 1895,[5] isolated from the thyroid gland an iodine-containing compound which he called "iodothyrin." He considered this the active principle of the gland.

* Read before the Historical Section of the Medical Society of the City and County of Denver.

Kendall, with thyroxin, made a more exact contribution to the thyroid physiology and therapy.[6]

Ivar Sandström, in 1880, discovered the parathyroid glands. He named them "glandulæ parathyreoideæ." A. Kohn,[7] in 1895, established them (Epithel Köerperschen) anatomically, genetically and functionally distinct from the thyroid gland.[7]

Eugene Gley, in 1897, proved by animal experiment their physiological importance, and that their complete removal was the cause of post-operative tetany.[7]

The foundation of scientific surgery upon a thorough knowledge of anatomy, pathology and physiology, and their reciprocal dependence, is exemplified in the development of surgery of diseases of the thyroid gland. Surgery of the thyroid gland is a composite of contributions of the civilized world, the French, Swiss, Germans, Slavs, Italians, English and Americans playing stellar rôles.

From the dawn of medical history, on through the early centuries, there were many handicaps common to all surgery. Little anatomy and nothing of pathology, physiology or bacteriology was known. In addition, there were the purely surgical difficulties, the control of pain, of hæmorrhage and of infection. When these were mastered, surgery became a respected science rather than an inexorable art.

In certain diseased conditions of the thyroid gland the greatest and most lasting benefit was, and still is, secured by surgery. No operation has been more highly standardized and no other productive of more brilliant results than the present so-called thyroidectomy; more properly termed partial or subtotal thyroid lobectomy. The evolution of the technic of thyroid surgery has converted one of the most hazardous into one of the safest surgical procedures.

The early operations were accompanied by a frightful mortality; 41 per cent. in 1850. Recent statistics show a fraction of 1 per cent. The dangers of the earlier operations were hæmorrhage, thrombosis of the jugular and subclavian veins, air emboli, injuries to the recurrent laryngeal and vagus nerves, damage to the trachea or œsophagus. The sequelæ were mediastinitis with or without abscess formation, phlegmon and fistula of the neck, erysipelas, pyæmia, tetanus, inflammation of the lung and pleura, tetany and cachexia strumipriva.[8] Death was due to hæmorrhage, either primary or secondary, or to the then almost inevitable sepsis.

Early surgery was imperative surgery resorted to only when the patient was *in extremis* from impending asphyxia or with a disorganized cardiovascular system. This was prior to the days of anæsthesia, before the antiseptic era, and, equally important, it was long before the development of adequate surgical instruments for the control of hæmorrhage, notably the hæmostatic forceps.

The improvement in surgical technic proceeded by stages, beginning with the introduction of general anæsthesia by J. C. Warren, October 16, 1846.[9] The next great advance followed Lister's epoch-making discovery of antisepsis, 1867.[9] Antisepsis was soon superseded by asepsis, 1870. Pasteur had

previously advocated dry sterilization of instruments and dressings.[9] Buchner[9] introduced the boiling of instruments in 1878 and in 1886 Schimmelbuch,[9] of von Bergman's clinic, inaugurated the practice of cleansing and disinfecting the hands.[9]

The hæmostatic forceps was developed from the prehistoric dental forceps. It first came into general use in the central European clinics in 1870 as the Schiebervorrichtung of Fricke.[10] The efficient control of hæmorrhage by means of the hæmostat replaced the crude cautery, the artery hook, the ligature carrier, the mass ligature and the crushing forceps. By these the field of surgery was vastly extended, delicate and deliberate operations became possible, elective surgery was born.

Before surgery as an elective procedure for diseases of the thyroid gland was advocated, there were a variety of methods of attacking the gland: the insertion of hair setons and canula to cause the disappearance of the tumor by suppuration,[11] incisions with drainage, the introduction of extracutaneous or subcutaneous mass ligatures, the application of chemical or the actual cautery, dissection cauterization, morcellement, evidement, the injection of iron, turpentine or iodine. About the middle of the nineteenth century, ligation of the thyroid arteries to induce ischemic atrophy, enucleation of nodules and cysts, transfixing ligatures with ecrasement and partial resection were recommended.

Roger Frugardi, of Salerno, 1170,[12] transfixed large goitres with shoe laces and permitted the ligated masses to slough.

Roger and Roland practiced the introduction of setaceum. When the goitre was adherent they encircled the mass with a shoe-lace ligature which was left firmly tied for two or three hours. The mortified mass was then cut away.[13]

Guy de Chauliac tunneled tumors with the actual cautery. Through the channel thus made he passed a heavy seton.[14]

The cure by the King's touch was practiced for over five hundred years, 1100 to 1600. Andre Dulaurens mentions that his king, Heinrichs IV, cured 1500 annually. Dulaurens, if nothing else, was an exemplary courtier.[15]

The first operation for goitre is credited to Albucasis, a Western Arabian of Cordova, Spain, about the year 1000. He used a crucial incision.[16]

Benjamin Gooch, 1770, reports two cases, both died of hæmorrhage. In one an unsuccessful attempt to control the hæmorrhage was made by digital compression exercised by relays of persons for eight days and nights.[17]

Adolph F. Vogel, 1771, operated on a case through a circular incision.[18]

The operation by Pierre Joseph Desault on May 20, 1791, is worthy of the first place in surgery of the thyroid gland if not in point of time, certainly in matter of technic.[19]

Jacquelin Hyon, female, aged twenty years, for seven years had trouble with her thyroid gland. In 1784, a mass formed in the right lobe, small at first then rapidly enlarged and became cystic. In 1788, it was lanced and drained of a yellowish serous fluid. The gland became adherent to the trachea.

Desault, through an anterior median longitudinal skin incision, exposed and double ligated the superficial vessels, then cut between the ligatures. The superior and then the inferior thyroid vessels were exposed, ligated and cut. The five-inch tumor was then grasped with a hook and pulled downward, mesially and laterally to mobilize the gland. It was then dissected free from the trachea, to which it was intimately adherent. For nearly sixty years this was considered an impossibility by the Swiss and German

surgeons. The patient's wound suppurated but she recovered and left the hospital in thirty days. Desault's case was the first in which the dissection was deliberate, the first in which the gland was dissected free from the trachea. He executed the essentials of thyroidectomy as it is understood today. It was many years before Desault's technic was improved upon.

Guillaume Dupuytren, January 1, 1808,[20] operated on a female, aged twenty-eight, who for eight years had a nodular three-lobed tumor of the thyroid gland. The central lobe four inches in diameter had been removed through a transverse incision by an unnamed surgeon of Paris. (This is the first mention of a transverse incision.) In the following six months the lateral lobes of the tumor had grown to such a size that respiration, deglutition and the circulation became greatly embarrassed. On three successive occasions the patient consulted and was examined by Dupuytren. Each time he refused to operate. The patient threatened suicide if no attempt was made to relieve her. Dupuytren capitulated to her insistent demands for relief. In Hotel Dieu on January 1, 1808, she was operated on. The teguments of the anterior surface of the middle of the neck were raised in a large transverse fold, then cut perpendicularly. The incision was enlarged to the symphysis of the chin above and to the sternum below. The tumor was exposed, the superficial vessels were for the most part avoided, others were double ligated and cut between the ligatures. The tumor was then retracted to the left and the right lobe was freed, its arteries were double ligated and cut between. The left lobe was treated in like manner. Then both lobes were elevated and under traction the adherent isthmus was dissected free from the trachea and removed. The trachea was markedly flattened. A sheaf of ligature threads was left hanging out of the inferior angle of the wound. The operation was long and tedious but was practically bloodless. The tumor weighed two and one-half pounds. The patient died thirty-six hours later.

Dupuytren called attention to the sensitiveness of arteries and recommended tying first the ligature on the side corresponding to the brain in order to avoid causing pain when tying the second or distal ligature. He was the first to observe the flattening and distortion of the trachea and stated that this was due to the prolonged pressure by tumors of the thyroid gland. A second time within a decade the French blazed the trail in thyroid surgery but years elapsed before that path was followed.

Paul Jule Tillaux,[21] on May 1, 1881, reports an interesting case with exophthalmos. A male, aged thirty-three, presented a marked pulsating thyroid with an audible bruit and a palpable thrill. There were decided pressure symptoms on the recurrent nerve and the trachea. Exophthalmos was progressively increasing. The pulse was rapid and a cardiac thrill was present. The patient's temper was irritable, he had nervous agitation with choreiform movements. On May 18, 1881, the patient was prepared for operation, chloroform anæsthesia was just begun when patient was seized with severe dyspnœa, breathing became harsh and cyanosis extreme. Operation postponed. Tillaux consulted the Society of Surgeons. The members were divided as to advisability of operating. The patient's condition was desperate and seemed doomed if denied the chance for relief. Tillaux, on May 21, 1881, with morphia and chloral analgesia under the Lister carbolic vapor spray, made a U-shaped incision. Hæmorrhage was controlled with hæmostatic forceps. (The first mention.) The sternomastoid and hyoid muscles were cut transversely at the turn of the transverse section of the skin incision which was over the lower third of the tumor. The tumor was exposed. On attempting to disengage and enucleate from below, the capsule was ruptured. Friable débris under pressure escaped. This diminished the size of the tumor, which extended downward beneath the sternum and laterally beneath the sternomastoid muscles. The capsule was dissected free from the trachea above and cut away. The cul-de-sac beneath the sternum was cleared of débris. Wound was closed and drained through the inferior angle. Lister dressing applied. Operation time one and one-half hours. He was placed in a specially prepared carbolized vapor room. Wound healed in ten days. Then erysipelas set in; he recovered from this on June 20, 1881. On July 27 he died from lung metastasis. Pathological

report by Bernard:—Sarcoma. This case was probably an exophthalmic goitre with sarcomatous degeneration.

Sir William Blizzard,[22] of Edinburgh, in 1811, was the first to ligate the superior thyroid artery for therapeutic purpose. The patient died one week later of secondary hæmorrhage and hospital gangrene.

H. G. Jameson,[23] of Baltimore, May 10, 1821, ligated the left superior thyroid with animal ligature. Patient cured. This was the first ligation in the United States.

H. Earle,[24] in St. Bartholomew Hospital, in a case of exophthalmic goitre on August 2, 1823, ligated the right superior thyroid artery and on September 11, 1823, ligated the left superior thyroid artery. On January, 1824, was reported restored to health.

Luiga Porta,[25] in 1835, ligated the thyroid arteries to induce ischemic atrophy of the thyroid gland. His first two single ligations in which he tied only one superior artery were without effect. In the third case both superior arteries were tied with marked, though temporary, benefit which lasted about four months. Porta concluded to secure permanent benefit both superior and inferior arteries on the same side should be ligated. July, 1850, through a single longitudinal incision, going between the sternomastoid and sternothyroid muscles, he exposed and ligated both arteries. This was the first ligation of the inferior thyroid artery. Porta proved the arteries of the opposite lobe are not capable of maintaining an adequate circulation in the lobe of the ligated side; further, ligation of the superior and inferior arteries in the same side may produce a radical effect.

Patrick Heron Watson, of Edinburgh,[26] considered the pioneer in Great Britain in 1874, reported five successful operations for thyroid disease with the following technic which had been used in 1861 by E. S. Cooper, of the United States:[27] long median incision, muscles separated, fascia of the gland exposed, superior pole mobilized with the finger. A threaded aneurysm needle was then passed beneath the gland from the mesial aspect of the upper pole to the middle of the lateral aspect of the lobe. This manœuvre was repeated with the remaining portions of the gland. The ligatures were tied and the mass was cut away with a curved scissors. This was over sixty years after the classic technic of Desault.

J. A. W. Hedenus, of Dresden,[28] in 1821, records six successful operations for extensive thyroid diseases. This record was not excelled for nearly seventy years. The success of Hedenus was a stimulus to surgery of the thyroid in Germany, but his followers for years failed to grasp the essentials of his technic. Hedenus used a vertical mid-line incision, exposed the gland, ligated the superior then the inferior thyroid arteries, freed the gland, transfixed and double ligated the isthmus. The mass ligation of the isthmus was practiced in Switzerland and Germany for many years following Hedenus. In modified form it is still used. Hedenus advised careful, gentle dissection to the posterior capsule of the gland, avoiding unnecessary and all rough handling of tissues, double ligation of the individual vessels as they are approached. In substernal goitre he used a sling of heavy thread passed through the tumor to facilitate delivery from beneath the sternum.

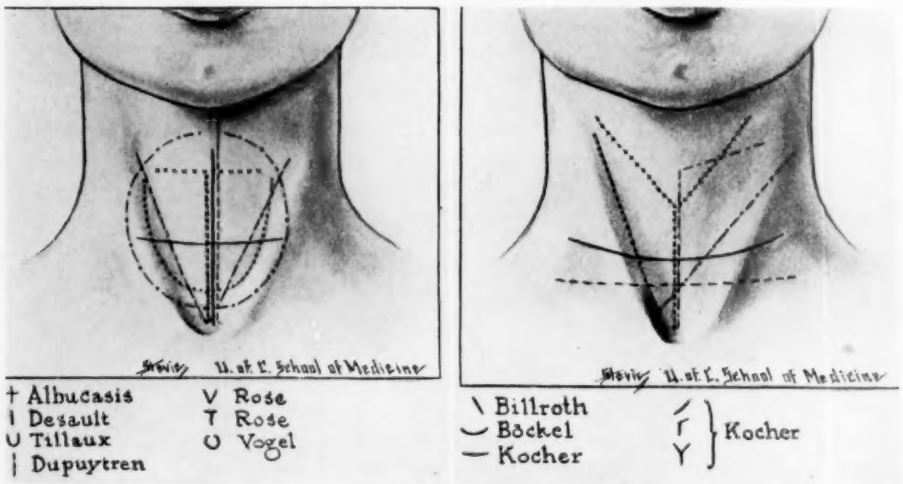
Victor Von Bruns, 1851 to 1864, had twenty-eight cases, mostly of cystic degeneration of the thyroid; however, two were carcinoma. One operation required four hours to complete. The instruments he used were several bistouries, dressing forceps, a scissors, one blunt aneurism needle, one hooked and one fenestrated forceps, several hooks, ligature rods, silk and catgut ligatures, water and sponges. Today, even the most resourceful operator would refrain from attacking even a simple goitre with so meagre a set-up.[29]

Dr. Charles Harris, of New York, in 1807, through a long mid-line incision, successfully extirpated a huge goitre of twenty-two years' standing by enucleating the mass piece by piece with his fingers and a knife; only two small arteries required ligation. The patient was well in three weeks.[30]

W. W. Greene, of Portland, Maine, is erroneously credited by some with the first radical extirpation of a goitre in the United States. By 1871, he had three successful

cases.[31] His first case was reported in 1866: Mrs. K., aged forty-five, tumor right lobe of thyroid, twenty-six years' standing, had never given her trouble until a year and one-half ago. Since then it had grown rapidly in size. Pressure symptoms were marked; dyspnœa, dysphagia and syncope. "Under ether anæsthesia a single lateral straight incision over the tumor from inferior maxilla to the clavicle was made. The sterno-mastoid muscle which spread over the tumor like a riband together with several fasciæ was divided on a groove director going to the capsule of the tumor, which, on being raised, bled profusely. The bleeding was controlled by digital pressure of an assistant. The tumor was covered with a network of large, delicate-walled veins which bled fearfully. With the fingers the tumor was separated, and the areolar attachments and the pedicle which contained three large arteries was reached. Each was tied separately with silk. When the last strand was tied the hæmorrhage ceased. The internal jugular vein which had been torn was also ligated. Wound was cleansed, closed by interrupted sutures. Patient recovered in thirty days. Weight of tumor twenty-four ounces. Time of operation twenty-two minutes."

Paul Sick, in 1867,[32] is credited with the first total extirpation of the thyroid gland and for being the first to observe the symptoms of operative thyroid deprivation.



Jacque L. Reverdin, on September 13, 1882, read a paper before the Geneva Medical Association on hitherto undescribed sequelæ of complete thyroidectomy. He called the condition "myxœdema ex-extirpatione gland thyreoideae" (myxœdema operatoiré).[33] Reverdin was the first to differentiate the aponeurotic or surgical from the anatomical capsule. This is an important contribution to surgery of the thyroid.

Theodor Kocher,[34] in 1883, before the Twelfth German Surgical Congress, reported his results in 100 thyroidectomies, thirty of which developed symptoms of thyroid deprivation called by Kocher "cachevia strumi priva." He therefore counselled strongly against extirpation.

It is incomprehensible that the work of Schiff done in Geneva twenty-five years before should have been unknown to these two masters of thyroid surgery.

The phenomena was explained by Kocher as (1) a disturbance of the blood supply of the brain consequent to removal of the thyroid gland which at that time was supposed to exercise a controlling influence on cerebral circulation, (2) the removal of the thyroid gland altered the blood causing qualitative changes in the nutrition of the brain. Several years passed before it was the acknowledged result of disturbed physiological secretion.

Theodorus Billroth,[35] April, 1861, while at Zurich (1861–1867) performed twenty

operations for thyroid disease, eight of which died of sepsis. This experience caused him to give up the operation. In 1867, he was called to Vienna, where, with the improved management in the treatment of wounds by the method of Lister, he again took up the operation.

Billroth used a lateral incision parallel to the inner border of the sternocleidomastoid muscle. He divided the sternohyoid, omohyoid and sternothyroid muscles transversely. In 1870, the artery forceps came into general use, which greatly facilitated his technic and improved his operative results. His clinic was cursed with post-operative tetany and injuries to the recurrent laryngeal nerve. In thirty-one cases he reported 30 per cent. of nerve injuries. Post-operative tetany gave rise to much discussion. Weiss,[36] in 1883, advanced the hypothesis that it was due to hyperæmia and irritation of the anterior horn cells of the spinal cord consequent to the ligation of the inferior thyroid arteries which increased the flow of the blood through the vertebral arteries; also, as highly probable irritation of the sympathetic nerves due to the ligation of the many vessels which stimulated the vascular centers in the cervical spinal cord and medulla. Billroth dissented from these opinions and suggested that it was due to the division of numerous nerves supplying the thyroid gland. The latter work of Sandström and Gley proved for all time the anatomical and physiological importance of the parathyroid glands.

Important as was Billroth's work in thyroid surgery[37] (in the early 'eighties he did more than any other surgeon), his chief influence was the interest he aroused in, and the stimulus he gave to, that galaxy of very able assistants, who later became famous surgeons: Wölfler, von Mikulicz, von Eiselsberg, von Haberer, Kocher. Each made valuable contributions not only to surgery of the thyroid gland, but also to other fields of surgery, notably that of the gastro-intestinal tract. The justifiable pride of the illustrious master was excelled only by the undying loyalty of his renowned assistants.

Anton Wölfler first called attention to the danger of injuring the recurrent nerve when ligating the inferior thyroid artery. He revived the practice of ligating the thyroid arteries as a preliminary to the more radical operation. Ligation was previously performed to induce ischæmic atrophy in the gland. This procedure was found to be contraindicated in cystic, colloid, degenerated and calcareous types of goitre. It did produce striking improvement in the hyperplastic and pulsating vascular enlargements.

Von Eiselsberg, in 1892, was among the first to experiment with parathyroid transplants.[38]

Johann von Mikulicz Radecki[39] rigidly followed the teaching of his master, Billroth. He noted the frequent sequelæ of recurrent nerve injury, of tetany and cachexia strumi priva. These were not understood at that time, but attributed largely to rough handling of the tissues and injury to the thyroid nerves. Compression of the trachea, when present, not only persisted but occasionally increased after removal of the lobe in the unilateral operations. To relieve this embarrassing situation, removal of the opposite lobe became necessary at the first or at a subsequent operation. Radical excision, described by Reverdin and Kocher as the cause of thyroid deprivation, was fully appreciated by Mikulicz as an operation to be avoided and justified only in cases of malignant disease of the thyroid. To obviate these unpleasant complications, Mikulicz devised his operation of bilateral resection, the so-called melon schnitt lobectomy, leaving only that portion of each lobe which is in relation with the posterior capsule and the inferior thyroid artery.

Mikulicz mobilized both lobes, ligated both superior thyroid arteries and the superficial branches of the inferior thyroid arteries, freed the anterior and lateral surfaces of the trachea, avoided dissecting too far posteriorly for fear of injuring the recurrent nerve. He then split the lobe longitudinally, removed the melon-shaped section, leaving only that portion of the gland and its capsule in the groove between the trachea and

œsophagus. This bilateral partial resection marked a decided advance in technic. It eliminated the complications which were hitherto common. With unessential modification it has been adopted wherever thyroid surgery is done. Commenting on his experience with the bilateral resection method he said: "I have had no complications and the convalescence was smooth. Whatever the function of the thyroid gland, be it a regulator of cerebral circulation, a blood-building organ, a gland with an essential secretion with important sympathetic nerve connection, the bilateral resection leaves a portion to continue to supply those functions. Damage incident to extirpation to the posterior lying structures, especially the recurrent laryngeal nerve, is most surely avoided." Had the rôle of parathyroid been known at this time he might have added: these structures are preserved.

A. Lücke,[40] of Berne, the predecessor of Kocher, was the authority on goitre before 1870. He advocated and practiced the parenchymatous injection of iodine. This procedure was attended with alarming and occasionally fatal consequences: iodism, paralysis of the recurrent laryngeal nerve, sudden death from embolism and thrombosis, œdema and closure of the glottis.[41] For a time he opposed ligation of the thyroid arteries and excision except for freely movable or pedunculated tumors. He revised his opinion for in 1872 he published a report of ten cases, mostly of adenomata, with only one death.

C. Böckel, of Strasburg,[42] reported a case of sarcoma of the thyroid in which he performed a thyroidectomy using a transverse or single flap incision. In order to secure greater exposure he dissected the flap upward. Mention of transverse incision has been made before, but Böckel's was the first report describing it. The transverse incision was a long time coming into general use. Credit is usually given to Kocher. While he popularized it he did not use it until some years after Böckel's report.

August Socin,[43] of Basel, practiced the intraglandular enucleation of adenoma, a modification of the procedure of Porta. This operation was a blunt or finger dissection of the adenoma from within the gland. It was a rough and incomplete operation. Primary and secondary hæmorrhage and infection were more common than with the cutting operation of excision.[44] Kocher was opposed to this technic because it was not usually complete, the capsule was rarely seen and the many remaining nodules took on rapid growth.

Theodor Kocher,[45] a pupil of Langebeck and Billroth, in 1872, at the age of thirty-one, succeeded Lücke at Berne. He was conversant with and stimulated by the operative success of his predecessor. Kocher was a born student and keen observer. He accepted only those new ideas which after personal trial had proven their merit. He was among the first Continental surgeons to adopt the principles of Lister and did much to popularize the method. He was foremost in simplifying the process and in developing the aseptic technic.

Kocher studied the anatomy, especially the circulation of the thyroid, and demonstrated by the injection of colored fluids the vascular distribution to the gland and within the larynx and trachea. This established the reason for the catarrhal inflammation and œdema of the trachea which frequently follows thyroidectomy.

In his first two years as chief of the surgical clinic at Berne he performed thirteen thyroid operations. He said: "There are three types of operations for thyroid disease: (1) total extirpation, (2) partial thyroidectomy or resection, (3) enucleation."

He was then using the median and the oblique lateral incisions of Billroth, whose technic he closely followed. He removed the gland piece by

piece and with cysts sutured the capsule to the skin, leaving the wounds open. August 1, 1874, he did his first total extirpation on a girl, aged eleven. A few weeks after the operation she developed marked change in character, became dull, sluggish and sullen. He stated: "It is a question whether there is a connection between mental deterioration and extirpation of the thyroid gland." Reverdin's report, in 1882, on two cases with "myxœdema ex-extirpatione gland thyreoideae" prompted Kocher to reëxamine all of his operated goitre cases, 101 in number. Seventy-seven were alive, seventeen did not report. Of the sixty remaining, five had carcinoma of the thyroid, two died of unrelated intercurrent illness, nineteen reported by mail. Those with unlateral excision were for the most part enjoying good health. The thirty-four total resections examined personally were less favorable. "One had tetany, sixteen showed varying grades of progressive mental and physical deterioration and changed physiognomy (old facies). They were sensitive to cold, anæmic, sluggish of speech and movement, showed general œdema and had peculiar skin changes and falling hair." He compared this condition to cretenismus and called the syndrome "cachexia strumipriva." This experience caused Kocher to take a decided stand against extirpation and it was years before he performed bilateral resection.

This first example of follow-up study was illuminating not only to Kocher but to the entire medical world. The importance of critical follow-up studies should be emphasized in every hospital and clinic as one of its most valuable educational functions. The value of follow-up studies is a vital contribution to the medical and surgical profession scarcely second to Kocher's outstanding work in goitre.

Following the suggestion of Kocher, between 1880 and 1890 the school children of the canton of Berne were examined. Kocher urged the Swiss Government to boil the drinking water and to add iodine as a goitre-preventive measure. McCarrison years later in the Punjab confirmed Kocher's stand. More recently in the United States similar studies and recommendations were carried out by the Marine.[46]

In 1877, Kocher substituted fine silk for catgut. In 1878, he changed from the straight median to the oblique, and, in 1882, to the winkel or angulated incision. If circumstances demanded, he made it a Y-shape by adding another arm. He dissected the gland from the trachea which ten years before he considered difficult.

In 1890, he discarded all other incisions for the transverse or collar incision made in one of the natural folds of the skin. About the same time he gave up the use of antiseptics in his operation wounds, having used solutions of carbolic acid, zinc chloride, bismuth, bichloride of mercury and adopted the more simple aseptic technic. He also shifted from the extracapsular to the intracapsular attack on the gland, performing what he called an enucleation resection, leaving the healthy gland tissue in relation with the posterior capsule to avoid injury to the recurrent nerve.

Kocher, deliberate, deft and gentle, made precise anatomical dissection in every case. He cut the strap muscles, exposed the gland, double ligated the superior thyroid artery, placing a third ligature on the superior pole before delivering the lobe which was drawn upward, then, after clearly visualizing the inferior thyroid artery, ligated it at a point where it changes its course from the horizontal to the vertical, just mesial to the carotid artery.

His operations on intrathoracic goitre are important. He recognized pressure of the goitre as the cause of softening of the cartilages, distortion of the trachea and the consequent respiratory embarrassment.

Dupuytren, who first called attention to the distortion and softening of the trachea, thought the dimunition of oxygen was the cause of the goitre. Tracheotomy was occasionally performed as a precaution against asphyxia. The necessity for this can be appreciated since long standing and very large adenoma were quite common.

Billroth's clinic was troubled with tetany and injury or paralysis of the recurrent laryngeal nerve, but had few recurrences of the goitre. Kocher, on the other hand, rarely saw tetany, had few recurrent nerve injuries but did have recurrences of the goitre.

In 1917, before the Swiss Surgical Congress, he reviewed his entire surgical experience in thyroid diseases, reporting .2 per cent. mortality in ordinary and 2 per cent. in exophthalmic goitre.

Kocher is deservedly acknowledged the leading authority on surgery of the thyroid gland.

W. S. Halsted, than whom no man in the United States did more to stimulate interest in thyroid diseases or more to develop a standardized technic, began his studies in 1879, while he was in Vienna, with his work on the development of the thyroid in fish. In 1887, he began his experiments with thyroid transplants in dogs.[47] This work resulted in the discovery of histological changes typical of hyperplasia, and a correct histological interpretation of exophthalmic goitre. He was the first to administer iodine to prevent post-operative or recurrent hyperplasia. In 1909, his work on the parathyroids and their relation to tetany is unsurpassed. He found that parathyroid homographs would not live unless a considerable deficiency was created and proved, the life of a dog could be maintained by a section of parathyroid one-fourth of a millimetre in diameter, which, if removed, would cause the animal to die of tetany.

Halsted's refined technic of thyroidectomy, developed in conjunction with W. G. MacCallum, is founded on precise anatomical and physiological principles. In this respect he ranks next to, if not equal to, Kocher. Halsted, in 1879, popularized the use of the hæmostatic forceps in the United States. In 1884, he was among the first to use transfusion of defibrinated blood. In 1885, he became the pioneer in local infiltration and conduction anæsthesia, which greatly improved mortality statistics in thyroid surgery.[48] In 1881,

he introduced the rubber tissue drain and in 1890 rubber gloves replacing the cotton gloves recommended by Mikulicz.[49]

C. H. Mayo has had more experience in thyroid surgery than any other man in the world. Reports from The Mayo Clinic have been an important factor in disseminating an understanding of the surgical technic and operative difficulties, which, in turn, greatly improved thyroid surgery.

The work of Crile, in Cleveland, Lahey, in Boston, and Bartlett, in St. Louis, is also a prominent factor in making thyroid surgery safe and in developing a type of operation in the United States which is quite different from that performed elsewhere.

The variety, length and direction of skin incisions used in the operations for goitre were many, before the simple transverse or collar incision became the incision of choice. The incisions are illustrated in the drawing shown in Figs. I and II and collectively resemble a spider web.

One is forcibly reminded of the criticism of Edm. Rose, who used a V- or T-shaped incision[50] when he stated the older operations for goitre in which the thyroid was attacked like an ordinary tumor, reminded him of working as in a spider web, ligating and repeatedly re-ligating the same vessels until the margins of the tumor were reached, where the large parent veins were torn and massive hæmorrhage occurred, obscuring the field. Blind mass ligatures applied to control this hæmorrhage caused frequent damage to the important structures.[51]

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THYROIDITIS*

By Howard M. Clute, M.D. and Frank H. Lahey, M.D.

of Boston, Mass.

from the Lahey Clinic

Clinical and pathological studies of goitre patients have demonstrated that thyroiditis is a relatively frequent finding. The significance, therefore, of inflammatory processes in the thyroid and their relation to goitre formation, to the occurrence of hyperthyroidism and to the late appearance of myxœdema can not be overlooked. We have divided this condition into: I, Simple thyroditis; *A*, Primary in the thyroid; *B*, Secondary to generalized infection. II, Suppurative thyroiditis; *A*, Primary in the thyroid; *B*, Secondary to generalized infection. III, Chronic thyroiditis (including Riedel's struma); *A*, Primary in the thyroid; *B*, Secondary to general infection.

Simple thyroiditis, primary in the thyroid, is not uncommon. We have reviewed the records of forty-two recent cases seen in the past five years, and we have the distinct impression that there have been many other patients whom we have examined and considered as early colloid goitres who might well have fallen into this classification of simple thyroiditis. It has been our experience that simple thyroiditis is not a serious disease, either in its course or in its outcome. Over 50 per cent. of our cases have very clearly been associated with a preceding infection of the tonsils, the pharynx, the teeth or the upper respiratory tract.

The typical patient presenting simple thyroiditis will give a definite story of repeated attacks of tonsillitis or of a recent sore throat or laryngitis or an infected tooth. Usually this infection has begun to quiet down when tenderness and swelling are noted in the region of the thyroid gland. Very commonly an early symptom is pain on swallowing solid food. The tenderness may start on the left or right side of the thyroid and gradually spread to the opposite lobe, disappearing on one side as the process extends to the other side of the gland. Very rarely have we seen any evidence of difficulty in breathing in these cases. A low fever ranging from 99° to 100° F. is occasionally present in the early stages of simple thyroiditis. Rarely it may be more severe and may persist for many days.

Mild symptoms of hyperthyroidism are occasionally present. Thus in two of our cases definite toxic symptoms of mild degree were present and disappeared as the process improved.

On examination, the thyroid gland is generally found symmetrically enlarged, but only to a very moderate degree. It is slightly firm and gener-

* Portion of this paper read by Doctor Lahey at the International Medical Assembly, Milwaukee, Wisconsin, October 19, 1931.

Portion of this paper read by Doctor Clute at the American Association for the Study of Goitre, Kansas City, Missouri, April 9, 1931.

ally definitely tender. It is not adherent to the muscles. There is no pulsation of the vessels. In these early cases the basal metabolism is usually within normal limits. Rarely, however, it may be elevated to +15 or at most +30. It returns to normal, as a rule, as the process recedes.

The tenderness in the thyroid gland persists for eight to ten days and then gradually disappears and the entire disease runs a course of twelve to eighteen days. Any clinical evidence of slight toxicity which may be present disappears within two to three weeks. Rarely a recurrence of the process may arise. This occurred in one of our patients who had a simple thyroiditis which subsided and a month after recurred and went on to the formation of multiple abscesses.

Since the process of simple thyroiditis is a mild and relatively benign process, it is not remarkable that myxœdema following in later years is relatively rare. In our records only one patient has developed a later myxœdema following a history of simple thyroiditis with no operation having been performed.

The treatment of simple thyroiditis consists in putting the patient at rest for a few days during the acute stage, the application of an ice collar to the neck and the administration of codeine and aspirin for pain. Careful observation of the course of the disease in order that the possible need of surgical drainage of an abscess may be determined early in the course of the disease is important. It has been stated that in simple thyroiditis the administration of Lugol's solution is of value. It is presumed that in the presence of an inflammatory process in the thyroid there will be an accompanying hyperplasia which in turn may well account for the onset of mild toxic symptoms. Lugol's solution may be given to produce involution of this hyperplastic area and hasten the process of repair in the gland.

Suppurative thyroiditis, primary in the thyroid gland, is, in our experience, a much more unusual condition than simple thyroiditis. We have seen five cases of either discrete or multiple abscess of the thyroid gland in the clinic. The onset of suppurative thyroiditis is marked by symptoms of a clearly serious nature. Preceding the onset there had been a history of infection in the throat or upper respiratory tract in four cases. Infection of the thyroid appeared with chills, fever, and local tenderness. Not infrequently the fever rises to 102° or even 103° F. Repeated chills are not common, but may occur. Difficulty in swallowing is an early symptom; and the patient may find that bending the chin toward the chest makes swallowing markedly easier, since this position relaxes the pressure of the prethyroid muscles on the gland.

The thyroid gland is definitely palpable and moderately enlarged. It is extremely tender and is noticeably more tender than in simple thyroiditis. There is a distinct tendency for the process to arise in one lobe or even the upper portion or lower portion of one lobe, and for this part of the gland to be adherent to the overlying structures. Palpation, however, is very difficult

because it causes severe pain. Mild symptoms of hyperthyroidism may well arise in association with suppurative thyroiditis and were present in two of our cases.

The course of the disease is at times marked by the development of more serious difficulties. Loss of weight may be rapid and severe, due to the infection and to the difficulty which the patient has in swallowing sufficient food. Fever continues and in one of our cases persisted for two weeks before active surgical measures were permitted; the temperature rising to 102° and 101° F. each day and going below normal each morning. The patients appear septic with a peculiar pale yellow tinge to the skin. The abscess, if unrecognized and untreated, may rupture on to the surface of the neck or into some neighboring viscus, such as the œsophagus, trachea or mediastinum. Such an accident usually results fatally. Œdema of the larynx with suffocation or with less severe respiratory difficulty may occur. Bronchial pneumonia may also arise in association with the infection.

Suppurative lesions in the thyroid gland occur not infrequently in association with generalized infection. Thus we have seen one abscess in the thyroid in a patient with a septicæmia with hæmolytic streptococcus blood cultures. Abscesses of the thyroid have been repeatedly reported as occurring in the course of typhoid fever, pneumonia, puerperal infection, *etc.*

The detection of suppurative thyroiditis in the course of a generalized infection is usually possible by simple observation and examination. In septicæmia, however, the abscess may develop insidiously and reach a considerable size without giving any active symptoms. This was our experience in one case.

The treatment of suppurative thyroiditis is of course drainage. A free incision in the neck should be made, the skin flap lifted as in the usual thyroidectomy, the prethyroid muscles retracted and cut, if need be, over the site of the inflammatory process and the lesion dealt with under direct vision. In this manner a lobe showing multiple abscesses may be resected, a large abscess may be adequately drained or an infected adenoma can be completely removed. Furthermore, the adequate drainage so essential in these cases can be more certainly established if adequate exposure is obtained.

The outlook for recovery in suppurative thyroiditis, when it is a primary lesion in the thyroid, is good. When, however, the abscess is secondary to a generalized infection, the outlook is of course serious. After drainage of the primary infection, recovery is rapid and the process has been checked in every case that we have seen. Delayed operation, inadequate exposure, and incomplete operation, however, may well permit the process to continue and a serious or even fatal result to follow.

Under the heading of chronic thyroiditis we may group many patients. Thus, we have been able to collect from our records forty-three patients with chronic thyroiditis, twenty-two cases of Riedel's struma, fifteen cases of thyroiditis with associated hyperplasia, two cases of tubercular thyroiditis and

two cases of syphilitic thyroiditis, a total of eighty-four cases of chronic thyroiditis, either primary or secondary in origin.

The etiological factors involved in the production of chronic thyroiditis are not as clear as those preceding the onset of simple and suppurative thyroiditis. In a very definite group of patients, however, preceding infection in the tonsils, teeth and throat seem to bear a definite relationship to the later occurrence of chronic inflammation of the thyroid gland. In certain cases it would seem from the history that a preceding acute thyroiditis had been present which subsided spontaneously, leaving a chronic inflammatory process in the gland. It is logical to assume that chronic thyroiditis is but the late stage of an infection in the thyroid which has not subsided, but has gone on to the production of increasing amounts of connective tissue and in the late stages (Riedel's struma) nearly an entire loss of all secretory structures in the thyroid gland. Under the stimulation of an inflammatory process in the thyroid gland, hyperplasia of certain thyroid follicles results. We have in our series seen fifteen cases of marked thyroiditis with definite hyperplasia of the surrounding tissue. Of these fifteen patients, twelve were diagnosed clinically as primary hyperthyroidism or adenomatous goitre with hyperthyroidism. They showed high basal metabolism rates and clinically were thyrotoxic. All fifteen cases were operated upon, a subtotal thyroidectomy being done in fourteen and a hæmithyroidectomy in only one, and all made a good clinical recovery from the operation. In the follow-up of these cases, however, it is to be noted that, with two exceptions, in which the basal rates were +11 and +9, all the rates were below normal, varying from −6 to −36. In five patients of this group, all of whom had subtotal thyroidectomies, myxœdema developed post-operatively.

From our experience with this group of patients, we are impressed with the fact that definite symptoms of hyperthyroidism may and do arise in patients whose thyroid gland shows histologically marked thyroiditis with hyperplasia.

In reviewing the forty-three patients with chronic thyroiditis, of whom all but one were operated upon, we are impressed, first, with the difficulties which this group have presented in clinical diagnosis, and, secondly, with the frequency with which myxœdema follows operation. Thus, in these forty-three cases, twenty-one were diagnosed as single or multiple adenomata before operation and twelve had the same diagnosis at operation. Three were diagnosed as malignant clinically and four were diagnosed as possibly malignant at operation. Of the group, twelve were diagnosed as thyroiditis clinically and twenty-four were diagnosed as chronic thyroiditis at the time of operation.

Myxœdema developed in fifteen of the forty-three patients with chronic thyroiditis. In one of these patients no operation had been performed. In one, a biopsy only was performed; in five patients, either a hæmithyroidectomy or excision of an adenoma was done, and in the remaining six cases a subtotal thyroidectomy was performed. Such an incidence of myxœdema in this group of patients with chronic thyroiditis makes it apparent that when

the condition can be recognized, an operative procedure should be employed which will relieve the symptoms of which the patient complains, establish definitely the presence or absence of malignancy, and leave as much thyroid tissue—poor though it may be—as is possible, for the future maintenance of thyroid function to protect the patient against possible myxœdema.

In 1926, Smith and Clute reported five cases of Riedel's struma from this clinic. The subsequent history of these five patients shows that two developed definite myxœdema, two are apparently well, and one died with malignancy in the thyroid gland. The microscopical sections from this patient, who later developed malignancy, were reviewed by many pathologists and opinions were about equally divided as to its being Riedel's struma or malignancy. The final outcome of the patient demonstrates that the true diagnosis was malignancy and shows the great difficulty which pathologists have in separating marked Riedel's struma from malignancy.

Since 1926 there have been seventeen additional cases of Riedel's struma in the clinic, making a total of twenty-one cases which we may report at this time. In these twenty-one cases, seven, or one-third, developed myxœdema after operation. One died at home of pericarditis, and thirteen are now known to be well. It is of interest to note, however, that the basal metabolic rates taken a year or more after operation in nine of these thirteen patients are all low, although they have no clinical myxœdema. Their rates are from −3, the highest, to −25, the lowest.

In Riedel's struma, which is histologically a thyroiditis of most extreme degree, with almost complete replacement of thyroid tissue by round-cell infiltration, myxœdema develops much more frequently than in chronic thyroiditis of lesser degree. It is significant that by basal metabolic examination and clinical findings myxœdema developed in seven of the twenty-one cases, and in nine of the cases definite low rates were present, though no actual myxœdema occurred. These findings make it most important that in patients with Riedel's struma as much thyroid tissue shall be left as is possible after relieving the patient's symptoms of constriction of the trachea.

We have had in our experience two cases of syphilitic thyroiditis. The first was a case of diffuse thyroiditis, clinically a chronic thyroiditis which was associated with a very marked narrowing of the larynx and upper trachea, and was accompanied by and probably arose from a mild laryngitis. The second case of syphilitic thyroiditis was apparently gummatous with a large adenoma-like swelling of the isthmus. A very marked syphilitic tonsillitis and pharyngitis and a positive Wassermann were present. Both did well with antispecific treatment.

There have been two cases of tubercular thyroiditis found on histological examination of operative specimens. Each case occurred in women, one of forty-five, and one of forty-seven, who on clinical examination presented apparently an adenoma of the thyroid. There were no toxic symptoms in either case. The adenoma was excised and each patient recovered with no

further difficulty. No myxœdema developed. No extensive conclusion can be drawn from these two cases.

The onset of chronic thyroiditis is slow and the time of its first appearance is generally not readily placed. In certain cases the hard, firm swelling in the neck is discovered accidentally by patient or physician. In other cases, the patient complains particularly of an uncomfortable feeling in the region of the thyroid gland, with some difficulty in swallowing. In the more severe types of chronic thyroiditis, particularly in Riedel's struma, dysphagia is the leading symptom. Tenderness over the gland is frequently present but is not outstandingly severe. In certain cases there is a low grade fever, with a temperature ranging from 99° to 100° F. and persisting for many days.

On examination, the thyroid gland in patients who had no previous goitre is symmetrically enlarged, very firm and hard. It is rare for it to be markedly adherent to the overlying structures, however, and the freedom of mobility of the entire thyroid in these cases is one of the few diagnostic points which distinguishes thyroiditis from malignancy.

The treatment of chronic thyroiditis is determined primarily by three factors: first, the necessity of arriving at a positive diagnosis as to the presence or absence of malignancy in many cases; secondly, the need of removing sufficient thyroid tissue to overcome the pain and pressure symptoms; and, thirdly, the need of operation to cure the hyperthyroidism which is occasionally present.

In patients who have symptoms of hyperthyroidism, but present a normal or low basal metabolic rate, operation should be delayed until the symptoms are more intense and the basal metabolism definitely elevated. In patients in whom the thyroiditis causes marked dysphagia, excision of the isthmus alone will tend to prevent the high incidence of post-operative myxœdema.

CONCLUSIONS

Acute thyroiditis rarely occurs as a serious prostrating condition. It occasionally progresses to abscess formation and requires adequate exposure and adequate drainage.

Syphilitic thyroidistis occurs as a diffuse thyroiditis or as a nodular gummatous thyroiditis. It is cured by antispecific treatment.

Tubercular thyroiditis is found occasionally on microscopical examination of thyroid tissue. It has little clinical importance.

Chronic thyroiditis frequently produces considerable constriction of the trachea with pressure symptoms and requires surgical relief.

An operation such as we have suggested (removal of the isthmus) relieves the constriction and does not produce myxœdema.

Myxœdema is particularly apt to follow operations on the thyroid for thyroiditis.

NODULAR GOITRE

By J. William Hinton, M.D.
of New York, N.Y.
FROM THE THYROID CLINIC OF THE NEW YORK POST-GRADUATE HOSPITAL

The term "nodular goitre" is gradually displacing "adenomatous goitre" and has a more significant meaning, as the latter is very misleading due to the fact it indicates a true pathological process, while the former refers only to the form and not to histo-pathology.

It is essential to understand that the different stages of goitre transformation do not represent distinct disease entities, as was formerly taught, and to accept the teaching that we are dealing with stages of a continuous process, as anyone who has studied the clinical and histo-pathological picture of the disease realizes that the different stages cannot be made to coincide clinically and pathologically.

The normal histological picture of different ages from stillbirth to senility have been studied[2] but the findings do not present a constant picture for people of a relative age. After a study of sections from the six groups, namely, stillbirths, infants, children from two to twelve years, adolescents from twelve to eighteen, adults from eighteen to sixty, and the senile group from sixty to ninety, in none of which was there a relatively constant picture except the stillbirths—from the study of these sections one cannot prognosticate the age of the individual from histological findings.

We are well aware of the classification which is generally given for goitres, but it is difficult for one to conceive of so many different diseases arising in one organ as have been described for the thyroid gland, particularly when the normal histology of the gland is so little understood. Therefore, for practical purposes, it would seem better to consider the cycle of thyroid diseases running according to the following diagram, which takes into account the different clinical pictures with the histo-pathology.

Normal

Adolescent or Colloid	Chronic thyroiditis
Nodular or Adenomatous	Hashimoto's disease
Exophthalmic or Graves' disease	Riedel's struma

Carcinoma

It is apparent to those who are constantly examining patients with thyroid disease that we are dealing with a transitional process, and it is difficult with

normal metabolic readings and a gland that is slightly palpable to state whether the enlargement is physiological or pathological, and whether treatment should be instituted or not.

Womack and Cole,[6] in a very recent publication, state: "Apparently the amount of change produced in the gland depends on the strength of the stimulus and the time it is at work and the amount of colloid or iodine that is present in the thyroid or that is easily available. Intense changes in the thyroid gland occurring during an infection can be almost completely prevented by feeding the animal large doses of iodine. Likewise, we have found it more difficult to produce glandular changes in the summer, when the thyroid is in a more complete resting phase and thus contains iodine. . . . Since it is possible to produce hyperplastic changes in the thyroid gland experimentally, and since it is likewise possible to cause an artificial involution by the use of iodine or a natural involution by the withdrawal of the stimulus, it occurred to us that it would be of value to study the anatomical changes that occur in the gland by a repetition of the cycle."

They used dogs for their experiments and in their summary state: "Following involution brought about by the disappearance of the stimulus causing the increase in function or by artificial involution due to the administration of iodine, replacement of fibrous tissue occurs. . . . Repetition of this physiological cycle may produce a nodular goitre similar to the so-called adenoma. The occurrence and location of these nodules is apparently dependent on the amount and the location of the fibrosis."

Keilty,[4] in a paper on the inflammatory nature of nodular goitre, states: "The purpose of this paper is to present the conception that many of the nodular thyroid glands should be considered as being inflammatory rather than as tumors. This is a part of a critical study of one thousand thyroid glands over a period of eight years. These cases represent the routine hospital admissions in central Pennsylvania. The cases include all forms of thyroid disease with the nodular types making up more than one-fourth of the group. . . . The clinical picture of chronic thyroiditis varies. The gland is always enlarged above normal, usually uniformly. Some parts are frequently more involved than others and in the sub-sternal type most of the enlargement may be below the sternum. The gland is predominantly nodular, the resistance is increased over that of simple hypertrophy. In the cystic types fluctuation may be apparent and in the smaller contractive forms the denseness of the calcareous and bony changes may increase the resistance. . . . Following the combined study of histories, gross specimens, and microscopical slides over a period of ten years, the opinion is expressed that a large proportion of the nodular thyroid glands, toxic and non-toxic, show the pathological evidence of chronic productive and contractive thyroiditis rather than adenoma." I have reported cases[3] to substantiate clinically what these authors have found true experimentally and pathologically.

The advice to a patient with a nodular goitre becomes clearer as its pathological picture is unfolded. The first step in an enlarged thyroid, whether it

is physiological or pathological, is the storage of colloid in the acini; the one exception to this has been the exophthalmic goitre, but it would seem that even in this type of goitre there is a colloid stage which may not have been detected by the patient, or the family physician, as it is well known that patients who are acutely ill from exophthalmic goitre may have no palpable gland and the size of the thyroid is no indication of its toxicity. So it would seem, because the gland in the exophthalmic type has not been noticed enlarged by the patient until the classical onset of symptoms, that there has not been a colloid formation preceding the date of history.

In some clinics it is taught that the adolescent type spontaneously involutes to normal in most patients without medication; also, that the colloid type that seeks treatment after several years' duration cannot be cured by iodine or thyroid medication, and this is due in many instances to the presence of an associated chronic thyroiditis with increase in interacinar connective tissue, but these cases are frequently benefited by treatment due to the absorption of the colloid from the distended acini.

The explanation of nodular goitre in most instances is due to the colloid stage involuting to normal in the major portion of the gland but leaving an area, or areas, of colloid encapsulated in connective tissue which is not detected on physical examination. But, when excessive demand is made upon the thyroid during the child-bearing period, the encapsulated colloid, not being able to meet the normal demand made on it, as the rest of the gland does, immediately enlarges, due to excessive secretion of colloid, and soon a nodular area is palpated in the gland. True adenomata of the thyroid arising from Wolfert rests do exist but they do not constitute over 10 per cent. of the nodular group.

The teaching has been that nodular or adenomatous goitres are not amenable to medical treatment and that harm is usually done if iodine or thyroid medication is given to this type, but cases have been reported[3] to show that this is not altogether correct. In most instances the nodular goitre does not respond to medical treatment, but, if the basal metabolism is normal and the nodules have been present only for a few months, there is no particular harm in treating this type of case with thyroid extract or iodine, providing the patient is kept under constant observation. After six or eight months, if no improvement has been noticed, then treatment should be discontinued, as no benefit will then be noted and the sooner the patient submits to surgery the better, as between 2 to 3 per cent. of the nodular group take on carcinomatous changes.

Comment.—We are indebted to Hertzler[1] more than any other individual for a clearer clinical and pathological picture of thyroid diseases, as he has had the opportunity to study the clinical cycle of the disease, and correlate the pathological process with the clinical picture which has given us a true conception of thyroid pathology. Rienhoff[5] more recently stressed the involutional phases of goitre pathology and it should be remembered that there are very few diseases that belong exclusively to surgery, but numerous

authors in the past have tried to make one believe that there is no place for medical treatment in the nodular or adenomatous goitre and it is exclusively a surgical problem. But if one selects the smaller goitres of recent origin it will be gratifying to see definite improvement in some, and actual disappearance of nodules in others. In cases that medical treatment will benefit, improvement should be noticed in the individual within six to eight months.

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LINGUAL THYROID

By Henry F. Ulrich, M.D.

of Philadelphia, Pa.

from the thyroid service of the university of pennsylvania hospital

Embryologists are practically all agreed that the thyroid gland arises from the fourth branchial pouch, as a median ventral invagination of the entoderm of the pharynx. This invagination is marked in later life by the foramen cæcum. The invagination is dragged down with the trachea, and, like the trachea, divides into the two lobes usually found.

The parathyroid glands have an anlage separated from that of the thyroid arising as paired structures from the entoderm of the third and fourth branchial clefts. Although they early attain positions adjacent to the thyroid, the parathyroids descend independently of the thyroid, which fact is consoling in the consideration of abberrant thyroid glands.

Developmental abnormalities of the thyroid are relatively uncommon. The migration caudalward, of the thyroglossal tract, may be arrested at any one of several positions in the line of its descent, such as: (1) Lingual, (2) sublingual, (3) suprahyoid, (4) infrahyoid, (5) aberrant lateral, and (6) normal. Other faulty positions after complete descent, such as retrotracheal and intrathoracic, are not uncommon.

It is the purpose of this paper to consider only lingual thyroid with a suggestion as to the management of the condition.

A review of the literature makes one agree with Cattell[1] who says that: "The least frequent of all aberrant locations of the thyroid is the lingual." He found that only two cases had been encountered in 7,600 operations on the thyroid at the Lahey Clinic. I find records of only two cases of lingual thyroid among over 4,000 patients with thyroid disease seen at the University of Pennsylvania Hospital. In 1925, Ashhurst[2] reported the only case of carcinoma of a lingual thyroid which I can find. In all, there are approximately one hundred cases in the literature. The relative infrequency of the condition is at once apparent. The follow-up reports on patients who have had lingual thyroidectomy are distressing. Post-operative myxœdema of varying degrees has been the rule. Lahey[3] feels that the development of post-operative myxœdema in these cases depends upon whether or not there is more thyroid tissue present. He reported a case of his own in a girl twenty-five years old, who developed myxœdema post-operatively. Hartley[4] concluded after his experience with a case which developed marked myxœdema after operation that the surgeon should interfere only when marked symptoms arise and only a minimum amount of tissue should be removed when a normally situated gland cannot be felt. He says: "It is important to decide whether the tumor is a true ectopia of the thyroid or merely an accessory

thyroid. The absence of a palpable isthmus favors the diagnosis of true ectopia."

The discovery of a lingual thyroid does not necessarily indicate active treatment. It might reasonably be expected to make the same response to physiological demands that a normally situated gland does, namely, enlarging somewhat in adolescence, fluctuating in size with the menstrual cycle, possibly increasing in size during an acute general infection and pregnancy. Rubeli[5] has reported an interesting case of a woman who was cognizant of a lingual thyroid first at puberty. It fluctuated in size with menstruation and attained such size during a pregnancy that tracheotomy seemed imperative. After Cæsarian section at term the goitre subsided to its former size and required no further treatment.

Smyth[6] found that the majority of reported cases occurred between the ages of fifteen and forty-five years, and felt that this was explainable by the fact that during this age period the thyroid attains its highest point of functional activity. I agree with Fetterolf,[7] however, that the majority of our patients are subjected to more careful examination during this period and that when lingual thyroid is present, it has been there since birth.

Treatment.—When a lingual thyroid attains such size as to produce urgent dyspnœa and dysphagia at any age, active treatment is indicated. In the young, tracheotomy should be the first step. In the mature patient it may or may not be necessary before thyroidectomy depending upon the dexterity of the surgeon and the degree of dyspnœa. When doing tracheotomy in the young patient, a large enough incision should be made to allow for an exploration of the neck to determine whether or not there is any normally situated thyroid. If any amount is found, one may with impunity proceed with lingual thyroidectomy and assume on the basis of experimental evidence that the remaining portions of thyroid gland will undergo hyperplasia and care for the normal metabolic activity of the patient. If normally situated gland is absent, it is imperative to adopt a conservative program. Such medical measures as are of use in the treatment of other physiological enlargements of the thyroid should be tried. In the presence of a low basal metabolic rate, mixed treatment with iodine and thyroid extract may be effective in reducing the size of the lingual goitre to the point where symptoms are relieved. If the basal metabolic rate is normal or high, iodine alone should be given. In event that medical treatment fails to reduce the size of the lingual goitre, thereby not relieving the obstructive symptoms, partial or complete thyroidectomy must be done. The electrosurgical knife may greatly facilitate this operation from the standpoint of its greatest technical hazard, *i.e.*, hæmorrhage. In the absence of other thyroid tissue, as determined by exploration, the excision of a lingual thyroid should be followed immediately by the administration of thyroid extract, regardless of the age of the patient.

I am particularly interested in that group of patients with lingual thyroids who have only mild or moderate symptoms referable to it. These patients should all be submitted to an exploration of the neck. The examination

of the neck by palpation so frequently leaves one in doubt about the thyroid gland that I believe it is to the best interests of the patient, the family doctor and consultant, to know whether or not there is any thyroid tissue in or about its normal location. Exploratory operation entails so little risk, while the findings at operation are so valuable for the proper management of a case of lingual thyroid that one need not hesitate to recommend it. The high incidence of myxœdema after excision of a lingual thyroid from a patient of any age and the potential danger of arrested development, both physical and mental, in the young, justify this means of learning as much as possible about the patient from a thyroid standpoint.

In this group of patients, no active treatment should be directed toward the aberrant thyroid if no normally situated thyroid tissue is found, which in my opinion will be the rule rather than the exception. The program here should be one of watchful waiting with careful follow-up, personally or through the family doctor, and the judicious use of iodine during the times of excessive physiological demands upon the thyroid gland.

CASE REPORTS.—The following case reports are from the service of Dr. Charles H. Frazier at the University of Pennsylvania Hospital in Philadelphia.

CASE I.—E. R. B., female, aged fourteen years, was admitted to University Hospital April 16, 1924, complaining of a tumor in her mouth. Sixteen months prior to admission she consulted her laryngologist because of some slight thickness of speech. He examined her for a return of tonsils and adenoids which he had removed four years previously. The only pathology found was a tumor at the base of her tongue. The child had never been conscious of its presence. A series of local remedies, the identity of which could not be determined, were applied, without appreciable change in the size of the tumor. The patient was returned to her family doctor, who prescribed iodides. The medication was taken for one year, during which time the tumor did not increase in size. Dyspnœa had never been present. Frequently the child choked on food and drink. There had been no hæmoptysis. Physical and mental development normal to this point. Menses had been established for one year. No change in size of tumor noted during the periods.

Past Medical History.—Measles, mumps and chicken-pox as a young child. Pneumonia at five years. Influenza at eight years. She was a healthy, well-developed child. The only demonstrable pathology was a well-defined tumor mass situated far back on the tongue, in the mid-line. Its color was red and contour smooth. It was moderately firm, was not tender and did not bleed when touched. Its posterior border was just anterior to the epiglottis. Its upper border was level with the highest point of the surface of the tongue. Examination of the neck by palpation revealed nothing suggestive of isthmus or lateral lobes of the thyroid. Basal metabolic rate was minus 8 per cent.

Through the regular thyroidectomy incision, the neck was explored (Dr. Francis Grant) April 26, 1924. Nothing in any way resembling thyroid tissue was discovered. The wound healed promptly and the patient was discharged May 1, 1924, without medication.

In spite of repeated follow-up requests the patient was lost until April 17, 1931, when her physician wrote: "I have just had the opportunity of examining E. R. B. She is in robust health, now married and has two children. The lingual thyroid has possibly decreased slightly in size. She has no symptoms from it."

CASE II.—R. B., female, aged three and one-half years, was admitted to the University Hospital May 31, 1930, with a chief complaint of clearing her throat. She had

no other complaints. Birth and development had been normal. In his examination of the child's throat during an attack of tonsillitis, just previous to admission, the family doctor discovered a tumor on her tongue. He had not treated it before this hospitalization.

Past medical history included whooping cough and an occasional sore throat. Examination was negative except for the findings in the mouth. Tonsils were moderately enlarged. On the base of the tongue in the mid-line was a reddish mass, symmetrical in form and shape, the size of the end of an adult thumb. It was not inflammatory or cystic. Direct laryngoscopical examination showed the tumor to be located well above the attachment of the epiglottis on the anterior pharyngeal wall. (Fig. 1.) Our diag-

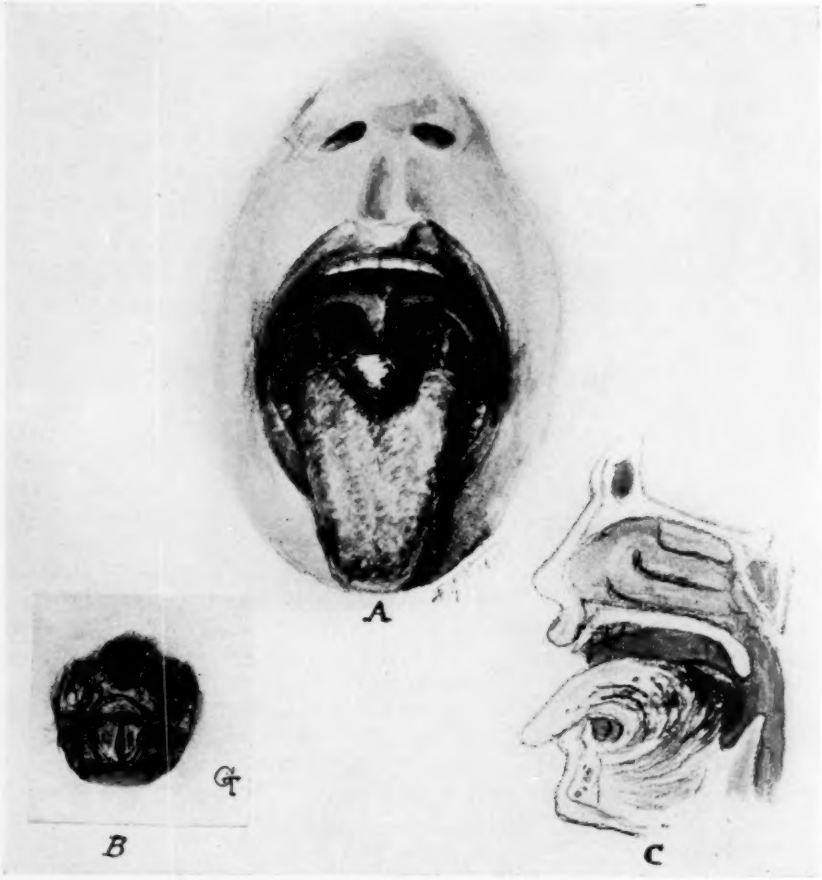

FIG. 1.—(Case II.) R. B.—A—Drawing showing tumor as it appeared on examination of mouth. B—Appearance of tumor at direct laryngoscopical examination, showing relation to epiglottis. C—Schematic drawing of sagittal section showing relations of tumor.

nosis was lingual thyroid. On June 6, 1930, the patient was operated upon (Dr. Henry F. Ulrich) under ether anæsthesia. The usual thyroidectomy incision was made, the ribbon muscles separated and a search for thyroid tissue was carefully made. None could be found. The wound was closed in the usual manner. The patient was discharged on June 11, 1930, without medication.

The last follow-up report from her physician March 31, 1931, says: "I have just examined R. B. She seems to be normal in growth compared to her other sisters. Her only symptom is slight pharyngeal irritation. The lingual thyroid has in my opinion decreased in size."

Comment.—Both of these cases represent that group of cases in which the symptoms are very mild. There was little doubt concerning the amount of thyroid tissue each possessed. The subsequent course of each, particularly the first, satisfies us that everything was gained for the patient and nothing lost as a result of our refusal to direct active treatment to the lingual thyroid. It is of special interest to note that the first patient has been subjected to the physiological demands of two pregnancies with no untoward symptoms referable to her thyroid.

SUMMARY

(1) A brief mention has been made of some of the unfortunate sequelæ of lingual thyroidectomy.

(2) It is suggested that all patients with lingual thyroid, when treatment is sought, should be submitted to an exploration of the neck.

(3) Patients with severe symptoms requiring lingual thyroidectomy should be placed on thyroid extract therapy immediately.

(4) A policy of watchful waiting is urged in cases of lingual thyroid with mild symptoms, especially if no other thyroid tissue is demonstrable.

(5) Two cases of lingual thyroid with follow-up notes are reported.

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CARDIAC FEATURES OF GOITRE*

WITH SPECIAL REFERENCE TO OPERATION

By John deJ. Pemberton, M.D.

Division of Surgery

and

Fredrick A. Willius, M.D.

Section on Cardiology, The Mayo Clinic

of Rochester, Minn.

The prominence of cardiac disturbances in goitre was recognized by the early writers on the subject, and as long ago as 1815 Parry[10] considered alterations in cardiac action and function associated with exophthalmic goitre. Similarly, Graves,[5] in 1835, von Basedow,[1] in 1840, Stokes,[19] in 1854, and Trousseau[20] in 1856, emphasized the cardiac features of goitre.

In considering the cardiac disturbances attending goitre we are concerned chiefly with exophthalmic goitre and with hyperfunctioning adenomatous goitre. Early observers, such as Potain,[14] in 1863, and Rose,[16] in 1878, described cases of heart failure and sudden death, presumably due to enormously large, nodular, and colloid goitres causing pressure on the veins and trachea. Cases of this nature have become so unusual that we deem it inadvisable to include them in this consideration.

Physiological Alterations.—The physiological changes which occur in both exophthalmic goitre and hyperfunctioning adenomatous goitre are mainly dependent on the increased basal metabolic rate. The most prominent cardiac effect of hyperthyroidism is excessive rapidity of the beat. An increase in metabolism is accompanied by an increased demand of tissue for oxygen; the demand is met by increasing the amount of air breathed each minute and by alterations in the circulatory system that favor an increased rate of flow of blood. Acceleration of cardiac rate is the first attempt of the body to increase flow of blood, and is a usual accompaniment of increases in basal metabolic rate.

Both exophthalmic goitre and hyperfunctioning adenomatous goitre usually are attended by alterations in blood-pressure. The most important of the changes in blood-pressure is increase in pulse pressure. In exophthalmic goitre the pulse pressure is slightly greater; average readings in the series of cases seen at The Mayo Clinic were 74 millimetres in exophthalmic goitre and 70 millimetres in hyperfunctioning adenomatous goitre. This increase in pulse pressure is affected, in exophthalmic goitre, by a slight rise in systolic pressure (to 147 millimetres†) and frequently a slight drop in diastolic pressure (to 73 millimetres), and in adenomatous goitre, by a decided rise

* Read before the Southern Surgical Association, December 8, 1931.

† The values for blood-pressure are averages obtained in readings of a large series of cases.

in systolic pressure (to 153 millimetres) which more than offsets a slight rise in diastolic pressure (to 83 millimetres).

Interpretation of these alterations in blood-pressure is facilitated by referring to previously conducted physiological investigation. Erlanger and Hooker's[4] work suggested the fact that the velocity of flow of blood was indicated by the product of pulse rate and pulse pressure, and von Recklinghausen held that the pulse pressure varied with the systolic output of the heart, provided that arterial elasticity was normal. Additional work has demonstrated that the minute volume output of the heart is increased in proportion to the increase in metabolism,[2, 8] and that an increase in stroke volume and minute output occurs in exophthalmic goitre.[15]

In a recent publication, Chang[2] described the results of his experiments on blood volume in exophthalmic goitre. He studied twenty-one subjects and found a definite increase in the volume of circulating blood. In applying this finding to clinical states he emphasized the fact that in exophthalmic goitre the blood supply of the thyroid gland was increased and that the rather extensive capillary bed of the neck may act as a shunt for a considerable portion of the blood. He commented on the similarity of this status with that occurring in arteriovenous fistula. Holman[7] has demonstrated that the gradually increasing dilatation of the vascular bed in arteriovenous communication is compensated for by a proportionate increase in blood volume, and that the volume is restored to normal by closure of the arteriovenous channel.

Thus, in cases of hyperthyroidism, clinical signs involving the circulatory system, such as tachycardia palpitation, increase in pulse pressure, the tendency to flushing and sweating, basal cardiac murmurs, and occasionally the occurrence of bruits in the peripheral arteries, are well explained by an increase in the rate of circulation.

Pathology.—In the hearts of patients who died in the active stage of hyperthyroidism, there are no distinctive histopathological changes. Wilson[21] has described lipoid changes and swelling of the muscular fibres, with indistinct striations. The myocardium is frequently pale, soft and somewhat dilated. These changes, however, are not pathognomonic of hyperthyroidism, for they occur in such diseases as pneumonia, pernicious anæmia, leukæmia, and the cachexia of carcinoma.

Considerable difference of opinion exists among clinicians regarding the occurrence of cardiac hypertrophy resulting from hyperthyroidism. Some maintain that cardiac hypertrophy occurs only when some primary and independent cardiac lesion exists, in itself capable of increasing the mass of cardiac muscle. We cannot accept this viewpoint, for in the series seen at The Mayo Clinic, numerous instances of cardiac hypertrophy have been demonstrated by necropsy (15 per cent.); increases have been noted of 100 to 200 grams beyond the accepted standard of Smith,[18] based on age, height and weight, in cases in which primary cardiac disease was absent. Furthermore, Simonds and Brandes[17] produced cardiac hypertrophy in healthy

dogs by experimental production of hyperthyroidism from feeding of thyroid substance. Our experience indicates that hyperthyroidism must exist a considerable period of time to produce cardiac hypertrophy. Furthermore, if the known physiological influences on the circulation of increased metabolism are interpreted in terms of increased work, it is not amiss to expect cardiac hypertrophy to occur in some cases. The effect on the heart muscle of thyroxin, either in excessive quantity or in abnormal form, is not understood, and conclusions concerning this aspect of the problem cannot be drawn at this time.

Clinical Features.—In examination of patients with hyperthyroidism, the most impressive cardiac finding is rapid and tumultuous cardiac action; this is usually more pronounced in exophthalmic goitre. The impression that the heart is definitely enlarged is frequently obtained, owing to the rapid, visible, wavy, and forcible apex beat. Dilatation to some extent probably occurs rather commonly, as was indicated by Wilson's[21] studies made of material obtained at necropsy. However, the overactive circulation in hyperthyroidism may erroneously suggest enlargement of the heart, and caution must be exercised in interpretation of existing signs.

Murmurs, systolic in time, are commonly audible in the cardiac area, and occur chiefly at the apex and at the second left intercostal space. They vary in intensity and in transmission. The murmurs are usually less intense when the patient is at rest, and become augmented under stress, indicating their close relationship to increases in rate of circulation. The apical systolic murmur may at times be the result of relative mitral insufficiency.

Unless caution is used, the presence of murmurs may erroneously be interpreted as being indicative of endocardial valvular disease. The most common erroneous diagnosis is mitral stenosis, particularly if the apical systolic murmur is rough and prolonged, thereby giving the impression of being presystolic in time. This false evidence may be supplemented by what appears to be a thrill resulting from the tumultuous cardiac action.

Endocardial valvular disease is associated with hyperthyroidism, but not as frequently as current diagnoses would indicate. When present, its incidence is greater in association with exophthalmic goitre than with hyperfunctioning adenomatous goitre, owing to the dominant occurrence of both exophthalmic goitre and endocardial valvular disease among patients of the younger ages.

Auricular fibrillation is the most common disorder of rhythm; it occurs in about a fourth of the cases of both of the diseases of the thyroid gland which are under consideration. It is present as a persistent mechanism in about 10 per cent. of the cases; it appears in a paroxysmal manner, with rapid rate, in about 5 per cent. of the cases, and it occurs intermittently, without unduly rapid rate, ultimately disappearing after the arrest of the disease, in about 10 per cent. of the cases. The persistence of auricular fibrillation following thyroidectomy is suggestive of the presence of associated

primary cardiac disease, residual cardiac injury from protracted hyperthyroidism, or recurrent hyperthyroidism of exophthalmic goitre.

When auricular fibrillation affects patients of middle life or later life, attention should at once be directed to the possible presence of thyroidism, particularly of hyperfunctioning adenomatous goitre. Not infrequently, patients are treated for a considerable period for what is believed to be heart disease, when in reality the cardiac phenomena are but the expression of unrecognized hyperthyroidism. Needless to say, the loss of time involved in such treatment may be the determining factor between chronic invalidism and death, or cure by surgical intervention.

The presence of auricular fibrillation does not necessarily increase surgical risk; it is frequently present when cardiac injury is minimal. However, the crucial points in determining surgical risk are the degree and extent of myocardial injury and the ability of the heart to adjust itself sufficiently to maintain a fairly normal circulation.

The occurrence of congestive heart failure in the course of hyperthyroidism has been the basis for considerable controversy. There appears to be a rather widespread belief that when congestive failure occurs it is evidence of associated and independent cardiac disease, and that hyperthyroidism itself is not capable of producing heart failure. The incidence of independent cardiac disease in patients with goitre is, of course, not unlike that of independent cardiac disease in patients of similar age groups who have diseases other than goitre. Nevertheless, that congestive failure solely as the result of hyperthyroidism does occur, even though its occurrence is infrequent, has been proved many times by careful correlations of clinical data and results of necropsy. Hypertensive heart disease and coronary sclerosis are not uncommon among patients with hyperthyroidism. These cardiac conditions occur most frequently in cases of hyperfunctioning adenomatous goitre owing to the similar incidence by age groups. The occurrence of angina pectoris in patients with hyperthyroidism has received considerable attention[6, 9] and recently Haines and Kepler[6] recorded their observations. They recorded distinct improvement in the anginal syndrome in most of the cases following partial thyroidectomy, and concluded that in their series, the risk was not so great as to preclude operation. Removal of the added work from the heart was believed to have been the basis for the improvement.

Preoperative Treatment.—When congestive heart failure is absent, the heart usually does not require special treatment. The exception to this is the heart with auricular flutter; if this condition persists after a reasonable period of rest and administration of compound solution of iodine[13] in doses of 10 minims three times daily, the use of quinidine sulphate is advisable. This drug, however, must be given with discretion, and twenty-four to forty-eight hours must be consumed in determining the patient's tolerance to it. It is our custom to administer 3 grains three times daily for this period of time, and if no idiosyncrasy to the drug is evident, the dosage is increased

to 4 grains every four hours day and night, until the flutter has been abolished. It is at times necessary to give as much as 30 to 40 grains in twenty-four hours.

Auricular fibrillation rarely demands special treatment. Unless complications exist, the period of preoperative rest rarely exceeds two weeks.

When congestive heart failure is present, the treatment is similar to that of primary heart disease without hyperthyroidism. However, digitalis should be employed with great caution, and ordinarily it is not used at once. Administration, by mouth, of ammonium nitrate in its enteric form, in doses of 6 grams daily, and intermittent intravenous injection of salyrgan (mersalyl), in doses of 1 to 2 cubic centimetres, usually suffices to rid the body of the œdema fluid and to restore cardiac function. When this method does not prove efficient, although it rarely fails, and when rapid auricular fibrillation persists, judicious use of digitalis is advisable. However, every effort should be made to avert toxic phenomena.

It should be recalled that the action of digitalis on the diseased heart of man is essentially twofold; the objections to its indiscriminate use are evident. Many actions ascribed to digitalis do not occur, or are purely secondary effects, resulting from improvement of the general circulation. Digitalis slows the cardiac rate by its direct action on the vagal endings, and to some degree by its action on the vagal centre. It is particularly effective in auricular fibrillation when ventricular action is rapid. It usually does not cause slowing of the pulse rate in cases of hyperthyroidism unless cardiac failure is an accompaniment. Digitalis increases the amplitude of cardiac contraction by its direct action on the myocardium. With these actions clearly in mind it becomes evident that indiscriminate administration of digitalis is undesirable in hyperthyroidism. Our experience has indicated that administration of the drug should be discontinued for at least four or five days preceding operation to insure the tissues' not being affected by its cumulative effects.

When cardiac function is restored, the patient should be gradually returned to limited activity before subjecting him to a surgical procedure. As has been repeatedly emphasized, it is unsafe to undertake operation on any patient who has been debilitated by a long period of complete rest. Under such conditions, circulation becomes sluggish, resistance lowered, and the patient is particularly susceptible to respiratory infection and venous thrombosis, the latter, of course, predisposing to fatal embolism. Furthermore, a short period of physical rehabilitation affords a test of cardiac reserve, for should heart failure again supervene under this program, it is fairly conclusive evidence that operation at that time was contraindicated. In such an event the need for prolongation of the period of preparation is obvious.

Probably in no other cardiac disturbances has treatment been followed by more brilliant results than those obtained by partial thyroidectomy in cases of "goitre heart." Certainly in no other cardiac disorder of such wide-

spread occurrence can complete and often permanent function be so promptly restored, with relatively little risk. The relief of the cardiac manifestations of arteriovenous aneurism by the permanent closure of the fistula is alone comparable. Presence of the more common cardiac manifestations of toxic goitre, that is, alterations in rate and rhythm, in the absence of congestive heart failure rarely constitute additional factors in the operative hazard, and accordingly do not usually demand any additional measures in the operative and postoperative periods. The complete and usually permanent subsidence of these disorders within two or three weeks following partial thyroidectomy is well known. A very large percentage of patients with congestive heart failure, who without operation are apparently doomed to a limited existence of chronic invalidism, will easily withstand partial thyroidectomy, subsequently regain complete cardiac efficiency, and enjoy many years of active and useful life. However, it should be clearly recognized that operation on these patients, as a group, entails a risk appreciably greater than if the hyperthyroidism is uncomplicated.

The relation of the liver to surgical risk in hyperthyroidism and in other diseases has not received sufficient consideration. The liver, one of the largest organs of the body, is likewise one of the most vital, and failure of its function is very serious. Much information has been gained regarding its functional integrity by the newer methods of estimation of function, particularly by the bromsulphthalein test. Impairment in hepatic function occurs frequently in hyperthyroidism, but knowledge of the pathological changes is as yet incomplete. Considerable degrees of atrophy of the liver are not unusual findings. Patients with retention of dye of high grade constitute very poor surgical risks, apparently indicating that the threshold of hepatic function is narrow, and that additional stress may be sufficient to cause death.

The debility of the patient, commonly proportionate to the duration of the hyperthyroidism, the degree of hepatic injury, and the basal metabolic rate are more accurate indicators of operability than the severity of the cardiac disorder. Patients who do not survive the operation rarely die of congestive heart failure, but more commonly of pulmonary infection, hepatic insufficiency, or arterial emboli.

In order to permit us to place quantitative values on the statements just made, we selected for review 100 consecutive cases of congestive heart failure accompanying exophthalmic goitre, and 100 consecutive cases of hyperfunctioning adenomatous goitre. The patients all had œdema of dependent parts; the minimal degree was Grade 2. The average duration of hyperthyroidism in the cases of exophthalmic goitre was 24.6 months and in adenomatous goitre with hyperthyroidism twenty-five months. The average duration of hyperthyroidism in patients with exophthalmic goitre who come to operation is about fourteen months.

Of the 100 patients with exophthalmic goitre, only one died of heart failure; this patient failed to respond to medical treatment and operation

was not attempted. Four patients died following thyroidectomy, death resulting from pneumonia in two cases, and from thyroid crisis in two. The latter two cases occurred before the period of the iodine treatment of exophthalmic goitre.

In the 100 cases of hyperfunctioning adenomatous goitre, death occurred in five cases following thyroidectomy. Heart failure was responsible for death in two cases, hepatic cirrhosis with insufficiency in one case, cerebral hæmorrhage in one case, and pulmonary embolism in one case.

We wish to emphasize the fact, previously reported,[12] that although it is possible, from a clinical estimate of the hazard, to select from among patients with goitre a small group (19 per cent.) who are handicapped, from which 81 per cent. of the total mortality will be derived, it is not possible to foretell accurately which individual patient will not survive the operation. Therefore, it is our opinion that when faced with the serious problem of deciding for or against operation on a patient who has marked decompensation of the heart and whose chances of recovery seem exceedingly remote, the duty of the conscientious surgeon is clear-cut: he should take into consideration that his estimate of the hazard is subject to error and that every patient should be given his one chance, irrespective of the risk involved.

Surgical Treatment.—Although a detailed description of the operative technic is clearly beyond the scope of this paper, we wish to stress certain principles which in our experience have proved of definite value. Owing to the fact that the margin of safety in many of the cases is exceedingly narrow, as sometimes the slightest mishap will mean the difference between success and failure, the need for the greatest possible care in every phase of the operation is obviously indicated. In the selection of the anæsthetic and the method of its administration there are two considerations of extreme importance: (1) Since all of the patients are more or less debilitated and, therefore, particularly susceptible to pulmonary infection, the type of anæsthesia which is least likely to contribute to this complication should be chosen, and, unquestionably, prolonged anæsthesia by inhalation should be avoided; and (2) the anæsthesia should be such that the patient can be awakened, in a reasonable state of comfort, after resection of the first lobe, in order that the functional integrity of the inferior laryngeal nerve can be determined. The value of this is obvious, and in our opinion it is the most important single step in the operation. It has been our experience that combined anæsthesia, namely, infiltration with procaine hydrochloride (0.5 per cent.), supplemented by nitrous oxide and oxygen by inhalation, most nearly fulfills these requirements. Under this method, the average duration of the administration of gases is from eight to ten minutes. For patients with obstructive dyspnœa, local anæsthesia is definitely indicated.

Not uncommonly, in cases of congestive heart failure, there may be circumstances relating to the condition of the patient or to the difficulties of the operation, such that performance of the operation in stages will materi-

ally minimize the hazard. The indications for this have previously been fully considered.[11]

Too often the surgeon is prone to believe that the outcome of an operation is favorably influenced to only a limited degree by any measure instituted after the patient has left the operating room, and it is true that a large proportion of these patients does not require any treatment other than symptomatic measures employed as a routine. However, not uncommonly grave complications develop, such as obstructive dyspnœa, hyperthyroid reactions, pulmonary œdema and infection, and since the successful treatment of these is dependent on early recognition of impending signs and prompt institution of proper treatment, close supervision by an experienced clinician is indispensable. It is for this type of complication, associated with cyanosis, that treatment by oxygen, preferably in the oxygen chamber or tent, has proved to be of great value.

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THE USE OF POTASSIUM IODIDE IN HYPERTHYROIDISM*

By Charles H. Frazier, M.D., Sc.D.

of Philadelphia, Pa.

From the Thyroid Clinic of the University Hospital, of Philadelphia

As goitre is not endemic in this territory, one would not presume the Thyroid Clinic to be of major importance, yet at the University Hospital we have records of over 4,200 cases. And as goitre is not endemic in this zone, the vast majority of the cases on our records are of the toxic variety. For some reason or other the incidence of toxic goitre is increasing notably year by year and the disease is developing more rapidly. It is also true that many more patients are being referred to the clinic in the incipiency of the disease.

The widespread use of iodine in the treatment of goitre in the last eight or nine years has caused the belief to be more or less general that this type of therapy is quite new, when in reality it is of very ancient origin. Sponge ash, which contains iodides, was used for its beneficial effect on goitre by the Chinese surely a thousand years before the Christian era. Hippocrates and Galen were familiar with its effect in goitre, as were many of the clinicians who practiced after Thomas Wharton accurately described the thyroid gland and gave it its name in 1659.

Iodine was first isolated by the French chemist Courtois,[1] in 1811. Nine years later, Coindet,[2] of Geneva, wrote of a new substance for the control of goitre. Soon reports appeared of the untoward effects of iodine therapy in certain types of goitre. Gairdner[3] described these symptoms which we now recognize as those referable to thyrotoxicosis, and Theodor Kocher,[4] in 1910, called this condition "Iodin-Basedow's."

For over one hundred years medical opinion was divided as to whether iodine should or should not be used in the treatment of any thyroid disorder. Within our own time I think we may justly say that its use was limited or given up entirely as a result of the influence of Kocher, who was definitely opposed to its use. Fortunately for the patient suffering from thyrotoxicosis, the pendulum has swung to the right as clinicians began to realize the import of investigations of physiologists and chemists in this very important field.

In 1896, Bauman[5] reported the presence of iodine in the thyroid gland, and isolated a substance which he called iodothyrin. Oswald,[6] a year later, found iodine in the thyroid colloid and stated that in general the iodine content of the gland varied with the amount of visible colloid. Fenger[7] found iodine in the thyroid gland of cattle as early as the third fetal month.

The investigations of Marine and his co-workers have been among the most noteworthy in this field. Marine and Williams (1908)[8] and Marine and Lenhart (1909)[9] published their investigations on the relationship of

* Read before the Philadelphia Academy of Surgery, November 2, 1931.

iodine to the histological structure of the thyroid in man and animal. They demonstrated conclusively that the iodine store in the thyroid was directly proportional to the amount of stainable colloid and inversely proportional to the degree of hyperplasis. The ability of the thyroid to store iodine was convincingly shown by Marine,[10] in 1915, when he reported that as much as 18.5 per cent. of a single dose of thirty-eight milligrams of potassium iodide administered to the dog by mouth could be stored in the thyroid within two hours.

In 1929, Dr. W. B. Moser and I[11] reported investigations before this society which confirmed Marine's findings, that the administration of iodine caused a rapid involution of thyroid hyperplasia with an increase of colloid in the thyroid acini. We believed, and still believe, that the improvement in the clinical picture of hyperthyroidism after iodine administration is due to the increased colloid formation under iodine stimulation, resulting in a flattening of the acinar cells.

It is impossible to discuss the entire history of iodine in relation to the thyroid, but one should not leave the historical aspects of this subject without mentioning that it remained for an American chemist, Kendall,[12] to isolate the iodine-containing hormone, thyroxin. Twelve years later, Harrington[13] gave this substance its proper chemical formula.

Although Oswald[14] and A. Kocher[15] had adequately described the effect of iodine therapy in exophthalmic goitre, it remained for Plummer and Boothby[16] to give this therapy a more exact status. It is due to their careful observations that this type of therapy as a pre-operative adjunct has become a rational part of the surgeon's armamentarium. Even before these workers had published their results, there were references in the literature which, had they been accepted, would have reduced the mortality after operations for hyperthyroidism considerably. Thus Cheadle,[17] in 1869, and again in 1875, reported that iodine therapy gave temporary beneficial results in Grave's disease. Loewy and Zondek,[18] in 1921, reported that small doses of potassium iodide definitely improved the subjective symptoms of the patient and caused a reduction of the basal rate.

The investigations of Plummer and Boothby were noteworthy because theirs was the first large series of cases in which metabolism studies were made. Although Plummer's concept of its action is, I believe, open to serious question, the accuracy of his clinical observations is unassailable. He believed that in Graves' disease the thyroid produces an incomplete thyroxin, and Gaddum[19] has shown that thyroxins containing less than four molecules of iodine have less effect on the basal rate than has the complete product.

Plummer and Boothby stated that they used "Lugol's solution (which contains 5 per cent. of free iodine, and 10 per cent. of potassium iodide) because it contained a large amount of iodine loosely combined." It would seem that they believed that free iodine was more readily absorbed from the gastro-intestinal tract than other forms of iodine.

The actual amount of thyroid iodine necessary for normal function is indeed small. The maximum storage of iodine per gram of dried weight is from five to six milligrams, and the maximum iodine content of the normal adult thyroid is from twenty-five to thirty milligrams. This has led many investigators to question the utility of using large doses of iodine in Graves' disease. Although Means[20] and his co-workers are probably correct in stating that small doses, a minim of Lugol's solution a day, will often give beneficial results in these cases, the fact remains that decided improvement in our experience does not occur in every case with such small doses. Furthermore, it should be stated definitely that iodine is not a cure for Graves' disease. Its effect is temporary, and advantage should be taken of its temporary beneficial effect for operative intervention. The continued use of iodine will cause a recurrence of the original symptoms, and, at this time, the histological structure of the gland will frequently show a markedly disordered structure.

Although the results obtained by Loewy and Zondek followed the administration of potassium iodide, clinicians in general have used Lugol's solution as suggested by Plummer and Boothby. Recently Lerman and Means[20] have shown that ethyl iodide by inhalation or iodide by mouth gave clinical improvement similar to that to be expected from the use of Lugol's solution.

During the past year, Cohn,[21] in the Laboratory of Research Surgery at the University of Pennsylvania, has given us additional information on this very important subject. He has, I think, conclusively proven that free iodine must be converted into an iodide before it is absorbed from the gastro-intestinal tract. The conversion in isolated gut segments takes place with exceeding rapidity. These latter observations we have recently confirmed in that we can find no free iodine in our solution fifteen minutes after it is placed in the gut.

Cohn studied the absorption of solutions of free iodine, iodides and Lugol's solution from different gut segments and found that on the whole the iodine is absorbed more rapidly when it is introduced as an iodide.

If the observations are applicable to the human, as they undoubtedly are, there is no reason why Lugol's solution should be continued in use. It is not pleasant to taste and frequently causes some gastro-intestinal discomfort. It only remained to be seen whether Loewy and Zondek's observations on the reduction of the basal rate could be confirmed in a study of a large series of cases. Since Lerman and Means' investigations were published this summer, the significance of Cohn's work has taken on a new aspect.

We have used sodium iodide exclusively on the thyroid service in preparing our patients with all types of hyperthyroidism during the past three months. Its effect has been just as striking as was the effect of Lugol's solution and the patients have not complained of the disagreeable effects of free iodine administration.

During the course of the investigation, we have operated on fifty patients, whose pre-operative medication has consisted of potassium iodide, sedatives, and such other therapeutic agents as were indicated. No Lugol's solution was used. For the sake of uniformity, all patients have received daily one cubic centimetre of a saturated solution of potassium iodide which contained one gram of the iodide. The pre-operative management of these patients did not vary in any other particular from that formerly used on the thyroid service. The usual time for preparation varied from seven to ten days. The time required was longer for decompensated patients. The use of patients for teaching and for other clinical investigations as well as delays in transfer from the medical to the surgical wards were other factors partly responsible for the average of eleven days which you will see in the records of cases that I will show.

In all of the cases there was a gratifying improvement in the general clinical picture, a steady decline in the pulse rate, and a decrease in the metabolic rate.

For the sake of comparing the effect of Lugol's solution and potassium iodide on the basal metabolic rate, we have compiled comprehensive tables of unselected cases of both types of toxic goitre, *i.e.*, hyperplastic toxic and toxic adenoma, showing the pre-operative decline in metabolic rate.

Table I shows the effect of Lugol's solution on the basal metabolic rate in hyperplastic toxic goitre.

TABLE I

Hyperplastic Toxic Goitre

Pre-operative decline of basal metabolism after administration of iodine.	
Average reading on admission	54.8
Average pre-operative reading	27.7
Average decline	27.1
Per cent. decline	49.4

Table II shows the effect of potassium iodide on the basal metabolic rate in hyperplastic toxic goitre.

TABLE II

Hyperplastic Toxic Goitre

Pre-operative decline of basal metabolism after administration of potassium iodide.	
Average reading on admission	55
Average pre-operative reading	29
Average decline	26
Per cent. decline	47.3

Table III shows the effect of Lugol's solution on basal metabolic rate in toxic adenoma.

TABLE III

Toxic Adenoma

Pre-operative decline of basal metabolism after administration of iodine.

Average reading on admission	39
Average pre-operative reading	25
Average decline	16
Per cent. decline	40 per cent.

Table IV shows the effect of potassium iodide on basal metabolic rate in toxic adenoma.

TABLE IV

Toxic Ademona

Pre-operative decline of basal metabolism after administration of potassium iodide.

Average reading on admission	31
Average pre-operative reading	17
Average decline	14
Per cent. decline	45 per cent.

We were interested to find that the figures we obtained in this small series of cases so nearly paralleled those of the much larger series of cases prepared with Lugol's solution.

To illustrate graphically the progress of our patients during their hospitalization, we chart daily the highest pulse rate recorded by the nurse. We also enter the metabolic rate under the day on which it was measured. The following cuts were made from such charts in our records of several representative cases. The pathological diagnosis confirmed our clinical diagnosis.

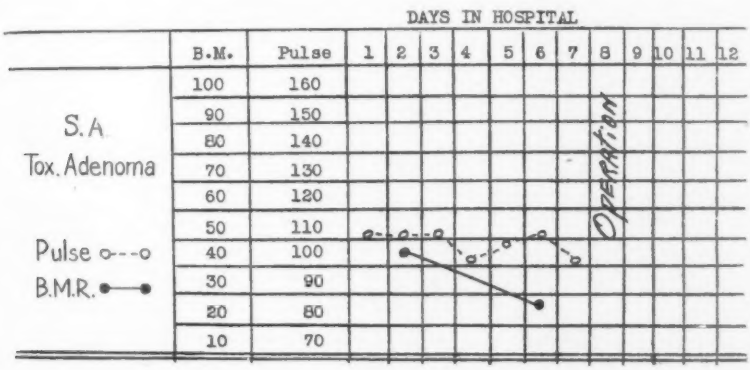

FIG. 1.

The first patient (Fig. 1) was a woman of forty-seven years of age. She was known to have had an adenomatous goitre for twenty years. Symptoms of toxicity had been present for six months before admission. Our diagnosis was toxic adenoma. There was nothing eventful about her course in the hospital.

The second patient (Fig. 2) was a woman fifty-four years of age. She was known to have had an adenomatous goitre for at least seven years with symptoms of toxicity for

six months. She had several abscessed teeth and infected tonsils. She had a subacute arthritis, probably infectious in origin, but without fébrile reaction. She had also a

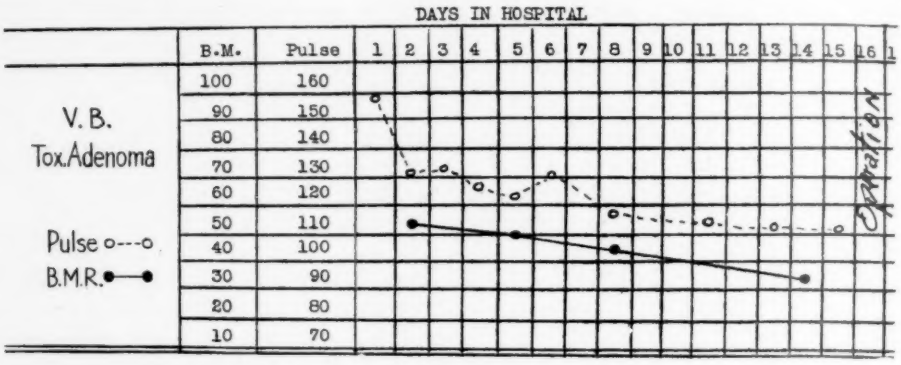

FIG. 2.

moderate degree of cardiac decompensation which prolonged her preparation. Her post-operative course was uneventful until discharge on the ninth day.

The third patient (Fig. 3) was an unmarried woman, thirty-eight years of age, who

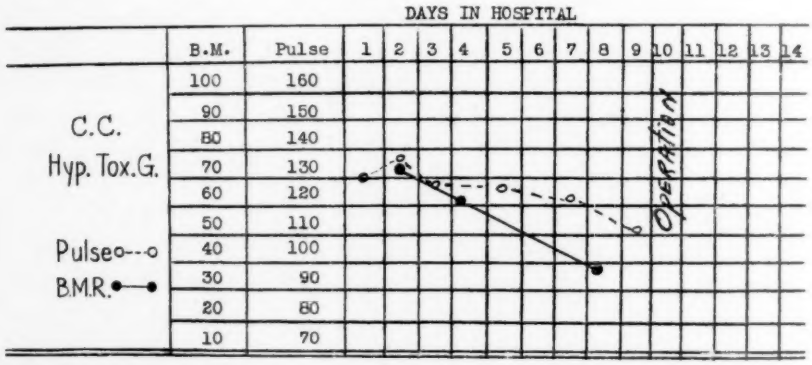

FIG. 3.

developed rather marked symptoms of thyrotoxicosis eighteen months ago. Thyroid enlargement was first noted four months ago. She had lost twenty-five pounds in weight. Exophthalmos was very marked. Our diagnosis was hyperplastic toxic goitre. She was

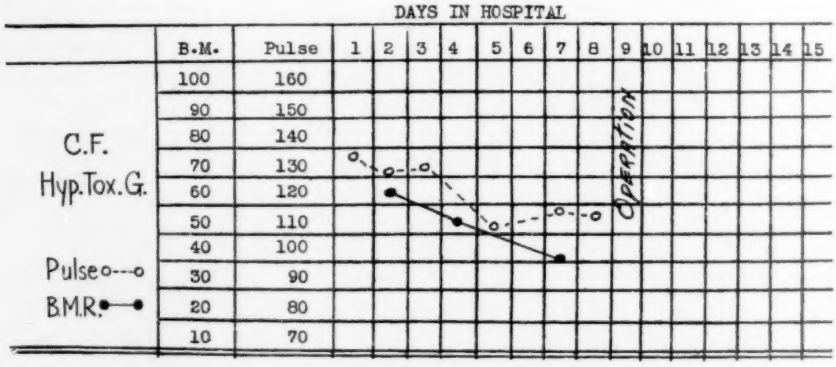

FIG. 4.

discharged from the hospital on her eighth post-operative day with a metabolic rate of plus 9 per cent.

The fourth patient (Fig. 4) was a married woman, thirty years of age, the mother of three normal, healthy children. The classical signs and symptoms of hyperplastic toxic goitre developed four months before admission and one month after the birth of her last child. Moderate exophthalmos had already appeared. Her clinical course in the hospital was entirely satisfactory. On the eighth day after thyroidectomy she left the hospital with a metabolic rate of plus 18 per cent.

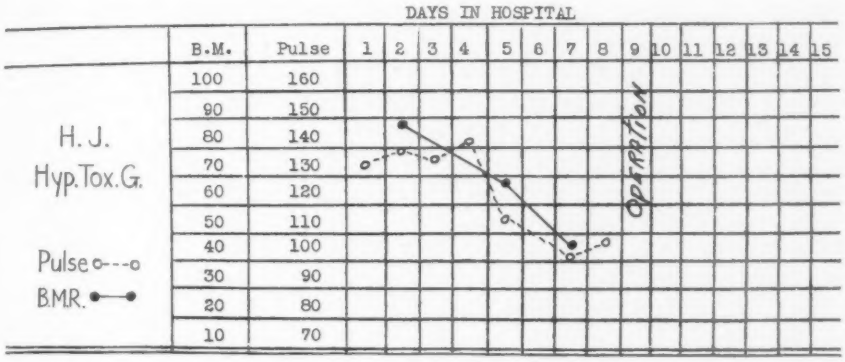

FIG. 5.

The fifth patient (Fig. 5) was a man, thirty-four years of age, who developed thyrotoxicosis seven months ago. Four months ago he first noticed thyroid enlargement and beginning exophthalmos. The latter had progressed until it was marked on admission. He had lost sixty pounds during his illness. He stood thyroidectomy well and left the hospital on the eleventh post-operative day with a metabolic rate of plus 1 per cent.

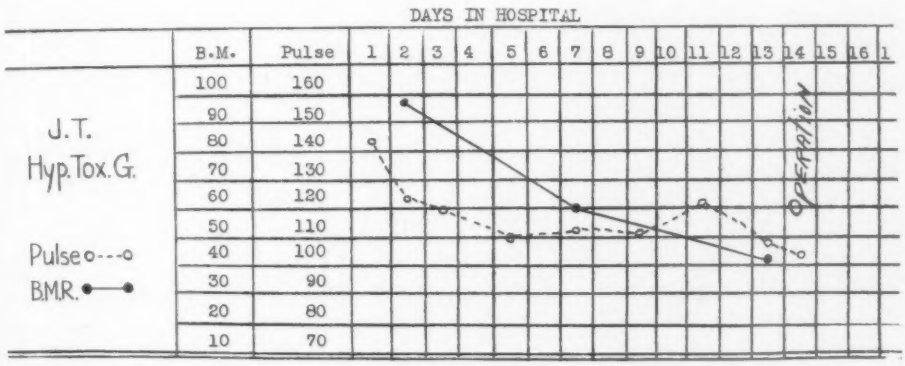

FIG. 6.

The sixth patient (Fig. 6) was a girl, twenty-two years of age, who said she had had thyroid enlargement since adolescence. Marked symptoms and signs of hyperplastic toxic goitre developed five months before admission. One month later her thyroid rapidly enlarged until it had the appearance of a large colloid goitre. Exophthalmos was severe. Because of her age and toxicity, her pre-operative preparation was slightly prolonged. She had a sharp post-operative reaction but left the hospital on the tenth day with a pulse rate of 90 and a metabolic rate of plus 16 per cent.

SUMMARY AND CONCLUSIONS

(1) A series of cases of both forms of toxic goitre is reported, which were prepared for operation with potassium iodide.

(2) The general improvement noted, as well as the specific improvement in pulse and metabolic rate, paralleled the improvement obtained by Lugol's solution.

(3) The clinical charts of several representative cases have been exhibited which graphically show the pre-operative response of thyrotoxicosis to potassium iodide.

(4) We conclude from the evidence obtained in our Surgical Research Laboratory that free iodine, to be absorbed, must be converted into an iodide, and from our clinical investigation, that it appears unnecessary to have free iodine "loosely combined," to which quality has been ascribed the effect of the administration of Lugol's solution on hyperthyroidism.

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A SIMPLIFIED TECHNIC IN THYROIDECTOMY

By Arthur W. Hoaglund, M.D.

of Minneapolis, Minn.

from the surgical service of St. Andrew's

In recent years thyroid surgery has ceased to be such a formidable procedure. It is no longer necessary nor advisable to submit the patient to a long tedious dissection. The long curved incision with a wide upward dislocation of the neck skin takes time, is unnecessary, and leaves a needlessly ugly

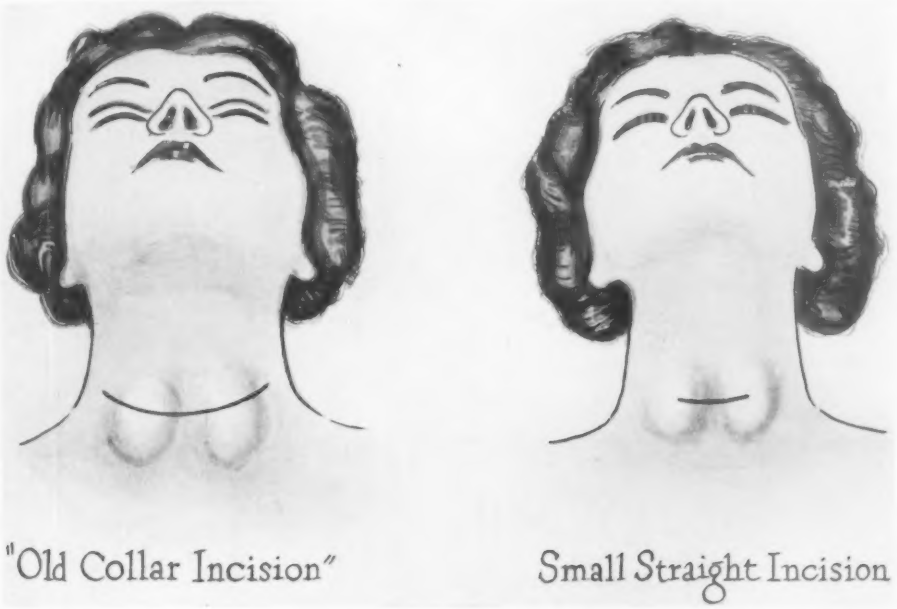

Fig. 1.—As 90 per cent. of thyroidectomy are performed in women the element of cosmetic appearance is an important one.

scar. The transverse division of the neck muscles is equally unnecessary except on occasional very large goitre or one that presents some exceptional technical difficulty. The following technic is simple, quick, and lessens the magnitude of the usual thyroidectomy.

A small incision is made straight across the neck, fairly low in relation to the gland—approximately three-fourths of an inch above the sternum. There is no need to curve the incision, as the normal anatomical curve of the neck will secure this appearance in the finished scar. Through this section of the skin and platysma, a wide undermining is accomplished. There is nothing of importance in this area to fear injuring, so that dissection may be rapidly performed. This freely exposes the underlying ribbon muscles of the neck, from the sternum to the thyroid cartilage and from one sternomas-

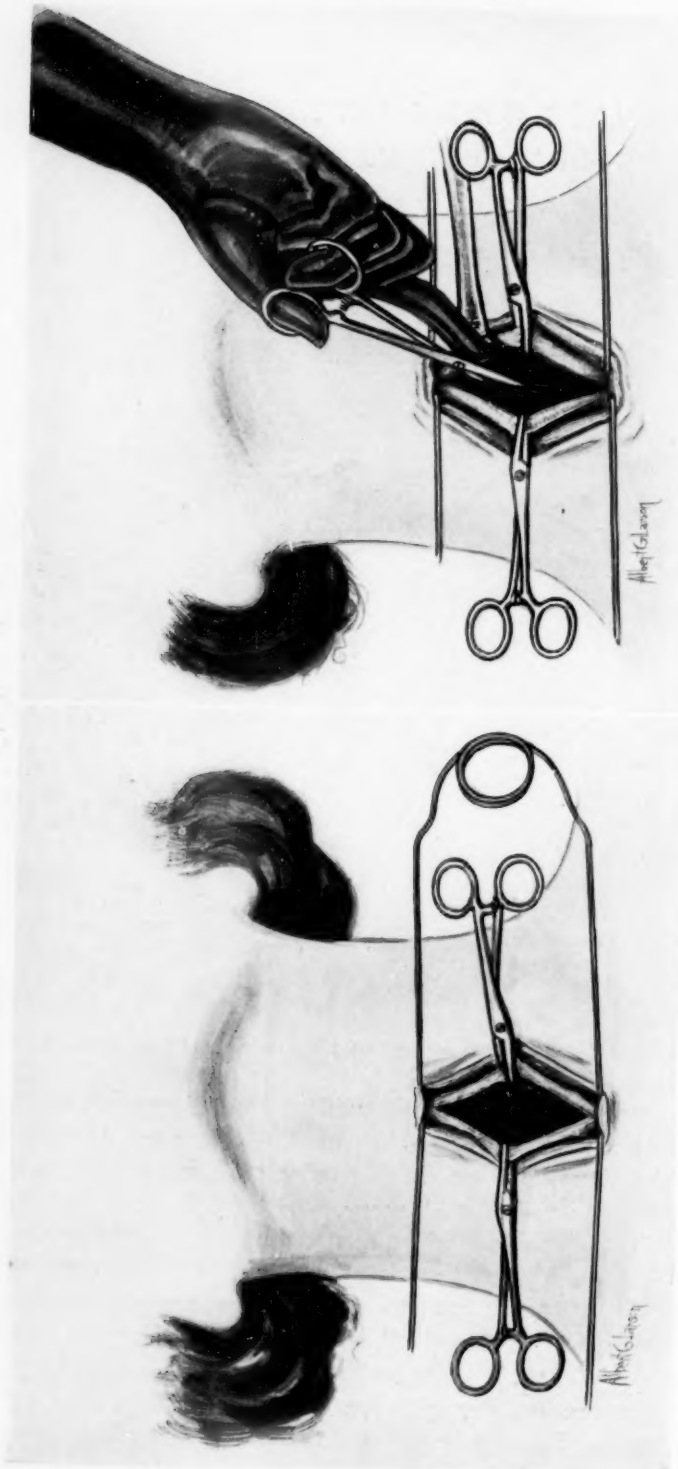

FIG. 2.—Showing room allowed with proper retraction. Any further lateral extension of skin incision would be entirely unnecessary.

FIG. 3.—Longitudinal division of pre-thyroid muscles.

toid muscle to the other. A straight median sagittal sharp knife separation of these sternohyoid and sternothyroid muscles brings one immediately to the anterior capsule of the thyroid. It is seldom necessary to divide the bellies of these muscle coverings. By gentle but thorough retraction, the entire gland may be exposed, especially when the subsequent steps of the operation delivers first one lobe and then the other through these separated muscle walls.

A finely pointed Kelly forceps, probed through the anterior capsule and spread, produces a wide opening through the capsule, which, being bluntly made, starts a well-defined line of cleavage from the underlying thyroid gland. By passing an index finger through this capsular opening and running it quickly over the upper lobe, around the lateral margin well behind and over the lower lobe, the thyroid gland is loosened entirely from its capsular setting. A Lahey clamp is then fastened into the anterior surface of the gland and the lobe in question is rotated out of its bed over the trachea. No pulling, force, or

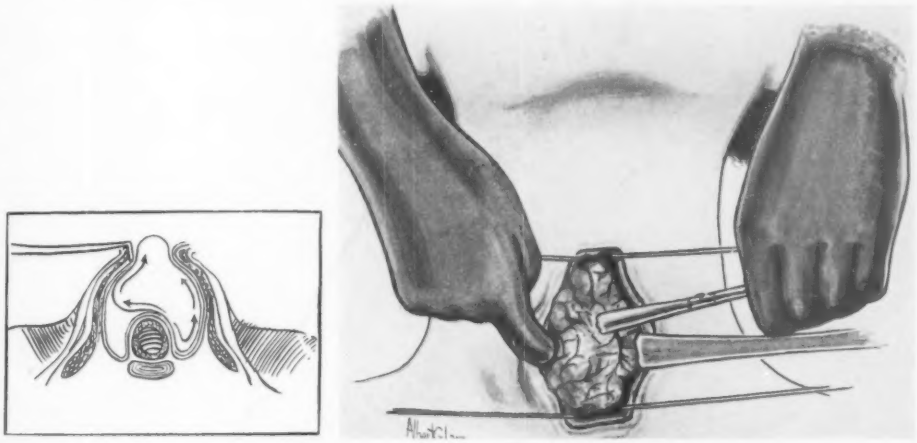

FIG. 4.—Blunt finger dissection and rotation of gland allowing complete delivery.

traction is necessary. A second Lahey clamp is then attached to the lateral surface of the partially rotated lobe and further and complete rotation is accomplished, which gives a full view of the entire lateral and posterior surfaces of the thyroid. If a substernal gland has been present, this should have been felt and delivered by the probing finger during the blunt dissection and freeing of that portion of the lobe. Here, then, is one lobe of the gland out upon the surface of our operating field, entirely within vision, and free for our every purpose. It is quite a simple problem to know how much of the gland will remain when the knife is passed through its substance. By fastening a line of clamps just posterior to this intended line of excision, and making special effort to fix the possible bleeding points, one is able to make a rapid removal of as much of this lobe as is deemed necessary. The question is not how much shall be removed, but how much shall be left for the patient's subsequent use? One lobe is completely dealt with. Ligatures are applied to all the bleeding

points and the second lobe is delivered and removed in the same manner. The operation is completed with the exception of suturing. If necessary a few sutures are fixed in the gland substance itself to be certain that hæmostasis is complete, and the capsule of the gland is sutured. Two small fine penrose rubber drains are placed, one on either side in the thyroid fossa and the ribbon muscles are joined in the mid-line by interrupted plain No. 1 catgut sutures. The skin and platysma are fixed by Michel skin clips which are to be removed

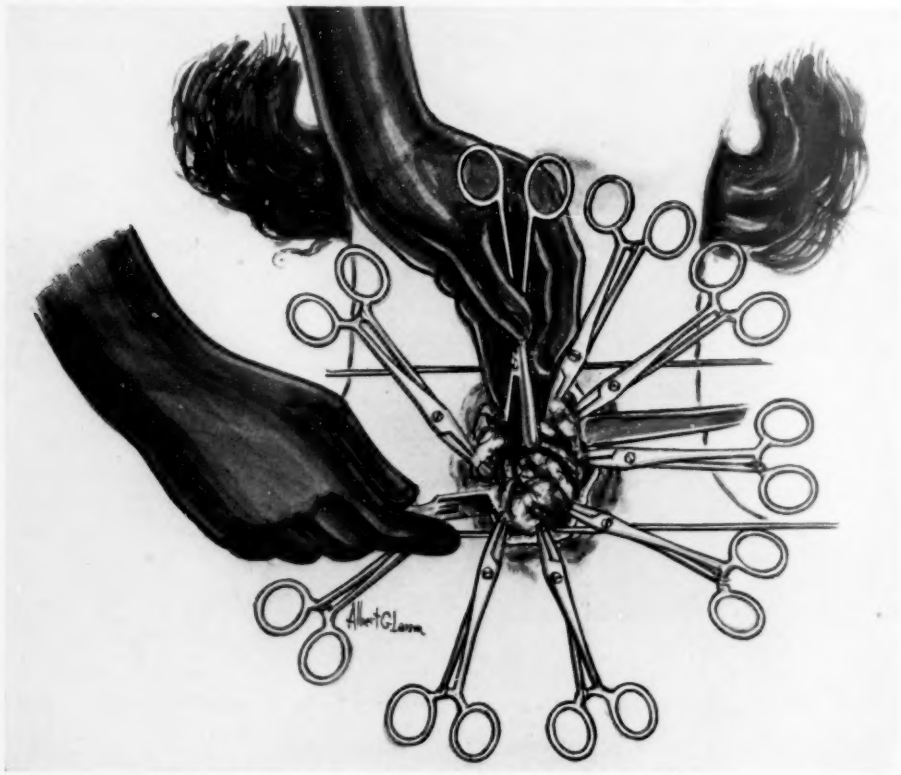

FIG. 5.—Simple excision of rotated and elevated gland. Control of hæmorrhage is now entirely on the surface and within vision.

on the second day post-operatively. The drains are to be removed within the first forty-eight hours. The patient is made as comfortable as possible with a neat bandage covering the wound and returned to bed.

Conclusion.—There is no occasion to attempt removal with the gland deep in the neck. Rotation makes a surface operation out of what many operators have made a deep dissection. Most glands are removed without splitting the muscles. Control of hæmorrhage is simplified. Time required is lessened and thyroid surgery ceases to be such a formidable procedure.

HOW MUCH THYROID TISSUE SHOULD BE REMOVED IN TOXIC GOITRE?*

By Frank H. Lahey, M.D.
of Boston, Mass.

The amount of thyroid tissue to be removed in toxic goitre varies quite widely in different individuals and different types of goitre. It is of very great importance that the essential medium be attained in thyroidectomy for toxic goitre between too great removal of thyroid tissue and the production of myxœdema and too little removal and the establishment of persisting hyperthyroidism. It is evident, therefore, that one cannot generalize about the amount of thyroid tissue to remove in terms of proportion of the entire gland. One cannot say that he customarily removes three-fourths, four-fifths, or five-sixths of the entire gland, and be in a sound position.

The attitude which everyone seeks to maintain in patients with hyperthyroidism is to remove enough thyroid tissue to produce a complete and lasting cure of the hyperthyroidism, but to leave enough thyroid tissue so that a myxœdema is not present.

Our experience with toxic goitre has demonstrated conclusively to us that the cure of this condition demands quite radical removals of thyroid tissue. Our experience with myxœdema, spontaneous and post-operative, has likewise taught us that this is an extremely undesirable state, and one that should not be considered lightly. Due to the fact that one can restore the basal metabolism rate to normal so readily with thyroid feeding, and due to the fact that patients so restored to normal basal rates are able to pursue practically all of their previous channels of life, one tends readily to assume the position that a certain amount of myxœdema is inevitable following thyroidectomy, does no particular harm, and should cause one no special concern. Such is not the case in our experience, and we feel strongly that the myxœdematous patients, even with their basal rates brought back and maintained at normal levels, are frequently not quite the same individuals physically and emotionally as they were before the production of the myxœdema. There is, in addition, no doubt, at various times, a variable demand for thyroid secretion in the body which is readily met by the organism's ability to increase or decrease output when the patient's thyroid or a part of it is functioning, but which is not met when the individual is on a fixed dosage of artificial feeding.

We should like to discuss, therefore, the amount of thyroid tissue to be removed in toxic goitre from the three aspects which relate themselves to this situation—the age of the patient, the character of the thyroid tissue to be removed, and the technical question of the removal of the thyroid isthmus.

*Read before the Southern Surgical Association, December 10, 1931.

First, as to the question of the age of the patient in connection with the amount of thyroid tissue to be removed in toxic goitre. One should have in mind always that the production of myxœdema in children is particularly undesirable, since thyroid secretion plays such a definite part in developmental life and psychic states. In doing subtotal thyroidectomy in children, considerable thyroid tissue should be left behind, and if an error be made, it should be on the side of leaving too much rather than too little thyroid tissue.

In connection with the question of involution of thyroid tissue and its probably lessened activity, it must be realized that the hyperplastic thyroids of children with primary hyperthyroidism involute just as definitely as do those of adults. (Fig. 1.) Just as in adults, so in children involution in the thyroid remnants and its effect upon the amount of thyroid secretion available must be considered in determining how much thyroid tissue to leave

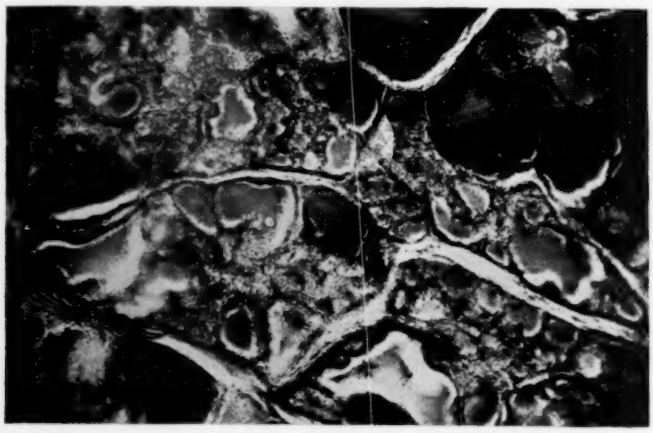

FIG. 1.—This is a microscopical section of the thyroid in a child of four and one-half years operated on for severe primary hyperthyroidism. Note that involution takes places with iodine just as readily as in an adult.

behind. Part of the process of old age is diminished thyroid activity, and in doing subtotal thyroidectomies on people well advanced in years, one should remember that it is probable that the functional capacity of the thyroids of elderly people is not that of younger individuals and so leave behind larger remnants than would remain in younger individuals.

The most important single factor which relates to the question of how much thyroid tissue should be left in subtotal thyroidectomy for toxic goitre is the question of the presence or absence of involution and its degree. Dr. R. B. Cattell, working in our clinic, in 1925, reported† on the effects of iodine feeding upon the histological picture of the hyperplastic thyroid tissue associated with hyperthyroidism. He found that when iodine was administered to patients with hyperthyroidism, definite changes in the form of colloid accumulation, distension of the acini, flattening of the epithelial

† The Pathology of Exophthalmic Goitre. Boston Med. & Surg. Journ., vol. cxcii, pp. 989-996, 1925.

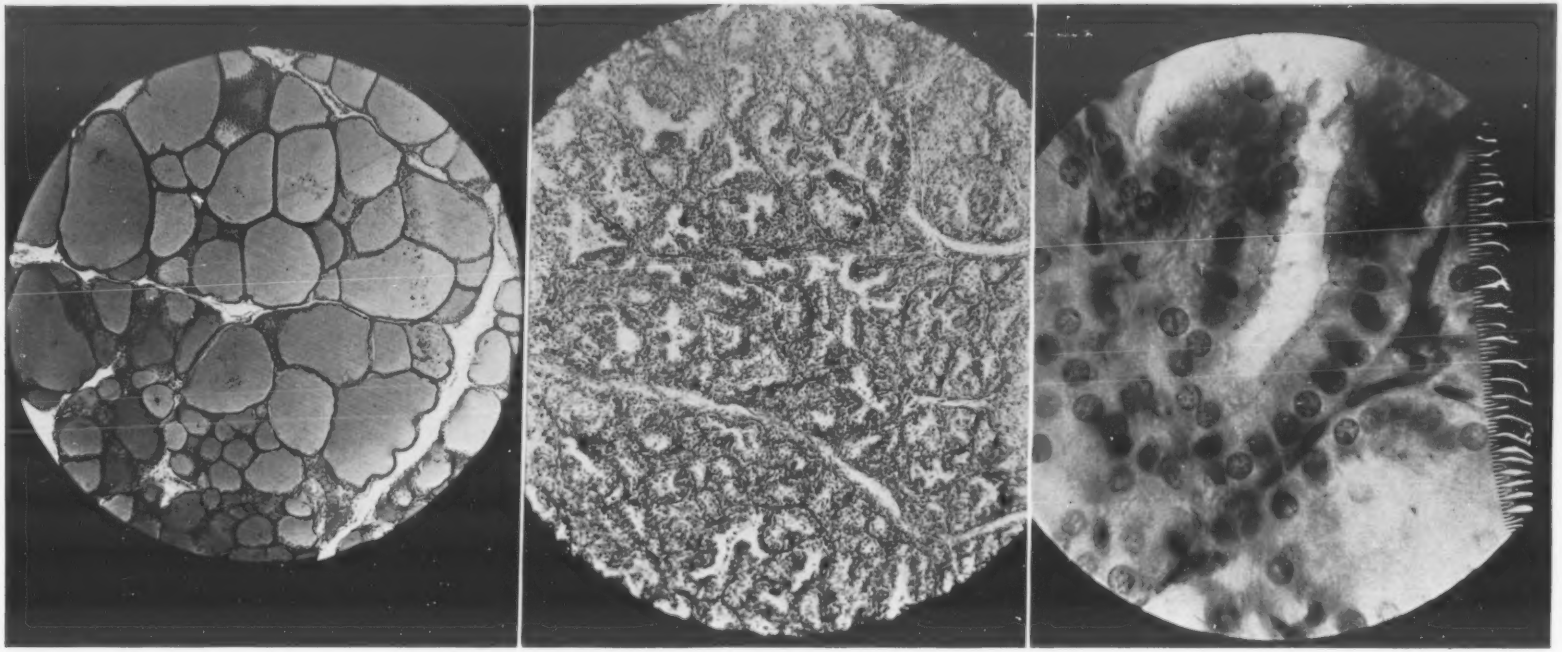

FIG. 2. FIG. 3. FIG. 4.

FIG. 2.—Showing marked involution following the prolonged administration of iodine. It is obvious that good-sized segments of involuted thyroid tissue of this type must be left if one wishes to avoid post-operative myxœdema. Involution to this degree will show its presence by gross evidence on cross-section and by clinical evidence in the way of a drop in basal rate, gain in weight, drop in pulse rate and improvement in nervous symptoms.

FIG. 3.—A microscopical section of the thyroid tissue in a patient with active primary hyperthyroidism. This is active hyperplastic uninvoluted thyroid tissue. It is obvious that but small segments of thyroid tissue of this type can be left if one wishes to avoid the possibility of persisting or recurrent hyperthyroidism.

FIG. 4.—A high-power microscopical section of an acinus and the high columnar cells lining the acinus in a patient with active primary hyperthyroidism. This is uninvoluted thyroid tissue of marked activity and one can readily realize that but small segments of tissue of this type should be left behind if one wishes to avoid recurrent or persistent hyperthyroidism.

cells lining the acini, and diminished vascularity usually occurred. This is the state which is termed involution, and one cannot observe the striking changes which occur following the administration of iodine without realizing that advanced involution must certainly be associated with diminished secretory activity, and without realizing, in determining the amount of thyroid tissue to be left behind after partial thyroidectomy, that the question of the presence or absence of involution and also its degree must play a part in settling this point.

Doctor Cattell found that out of all the glands he studied, 90 per cent. showed definite involution following the pre-operative administration of iodine, and 10 per cent. did not show involution. If one will look at Fig. 2, which demonstrates advanced involution, it will be evident that a good-sized remnant of tissue of this type must be left, if one is to avoid the post-operative onset of myxœdema. If, on the other hand, one observes in Fig. 3 the uninvoluted thyroid tissue with its limited amount of colloid storage, with its high columnar epithelial lining the acini (Fig. 4), with its papillary projections into the acini, it is evident that here is very active thyroid tissue, and if one hopes for a cure of the hyperthyroidism, very radical removals of tissue of this type must be undertaken. It is obvious that if segments of thyroid tissue of the uninvoluted type of a size similar to those of the involuted type be left behind, the hyperthyroidism will not be cured, persisting hyperthyroidism will result, and from these good-sized extremely active remnants will develop the occasionally occurring large post-operative recurrent goitres. It is evident, therefore, that in patients in whom involution of the thyroid tissue with iodine has not taken place, very radical thyroidectomies must be done, and but small thyroid remnants left behind.

Iodine involution or non-involution usually does not occur without clinical evidences of its existence or without gross macroscopical evidences of its presence when a cross-section of the gland is made at the operating table. (Fig. 5.)

Hand in hand with a good iodine involution of the gland during the eight to twelve days of pre-operative preparation with iodine, one usually sees a gain in weight, a drop in pulse rate, a drop in the basal metabolism, and an improvement in the nervous symptoms. This clinical evidence of involution of the gland and improvement with iodine is further confirmed by the gross appearance of such a gland when a cross-section is made of it at the operating table, and it is observed macroscopically. With well-marked involution, the cross-section of the thyroid, due to its accumulated colloid, will show it to be pale and œdematous-like, in contrast to its usual brownish-red and cellular appearance. Due to accumulated colloid, it will be much more firm than the uninvoluted gland. Due to the accumulation of colloid, while it will contain just as many blood-vessels, they will be flattened out by the pressure of the distended acini, and so on section it will appear less vascular. This will indicate good involution, and, in such cases, if good-sized remnants are not left behind, a high percentage of myxœdema will result.

In those patients in whom iodine involution does not occur during the eight to twelve days pre-operative period of iodine preparation (about 10 per cent. of the cases), there will usually not be a gain in weight or drop in pulse rate. The nervous symptoms will not materially diminish, and the basal metabolism will not drop, but at times will rise. On making a cross-section of such an uninvoluted gland at the operating table, it will be found to be reddish-brown in color, cellular and vascular in character, and unless, in this type of thyroid tissue, quite radical removals are done, resulting in leaving very small remnants of thyroid tissue, persisting and recurrent hyperthyroidism will ensue.

The occurrence of hyperthyroidism in association with the degenerative

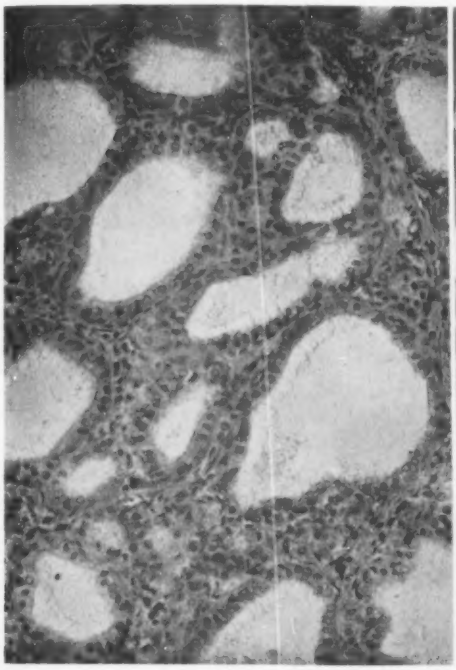

FIG. 5.

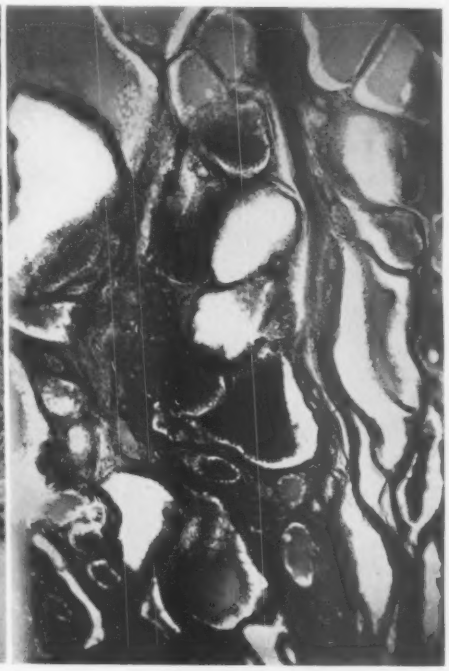

FIG. 6.

FIG. 5.—Moderate involution following the administration of iodine for but a short time. Note the accumulation of colloid and the appearance of lessening thyroid activity.

FIG. 6.—A microscopical section of a multiple colloid adenomatous goitre. Note inactive type of thyroid tissue and how necessary it is not to do too radical removals in thyroids of this character.

processes of hyperinvolution, which are associated with endemic goitre, and which have been termed multiple colloid adenomatous goitre, demands that in subtotal thyroidectomies upon thyroid tissue of this type, good-sized remnants must be left if one wishes to avoid the probability of a high percentage of myxœdema. One has but to glance at Fig. 6, showing this type of tissue, to realize that this is of a poor character, and that if too radical removals are done in such cases, many patients will develop post-operative myxœdema.

Up to recent years, one heard a good deal about the need of leaving a layer of thyroid tissue of the isthmus over the trachea in subtotal thyroidec-

tomy, in order to prevent reactions in that structure and consequent postoperative tracheitis. While this recommendation was quite general, we believe from our experience that it is not necessary, and, at least in our hands, tends to result in inadequate removals of thyroid tissue in operations particularly for primary hyperthyroidism.

We have now for the last few years purposely bared the trachea and removed all of the isthmus in all thyroidectomies for toxic goitre, in order that we might leave remnants of thyroid tissue only along the sides of the trachea, where they would protect the parathyroids and the recurrent laryngeal nerves. If radical removals of thyroid tissues must be done, and, with the above-mentioned discussion as to tissue type in mind, they not infrequently must be—then it is desirable to remove thyroid tissue only at points where it is not dangerous to do so. We have not observed any greater degree of tracheitis following complete removal of the thyroid isthmus and baring of the trachea than we saw when care was taken to leave a remnant of thyroid over the trachea. In fact, we have not only completely bared the trachea, but have almost always caught the remnants of thyroid on either side up to the trachea with stitches passed superficially through that structure, and we cannot see that it has increased the degree of postoperative tracheal reaction.

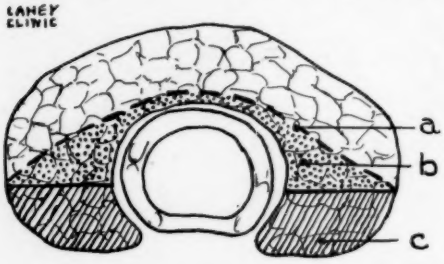

FIG. 7.—If a segment of thyroid is left over the trachea, only the tissue above line *a* will be removed. If the trachea is bared, it will be possible to leave only the shaded and lined section *c*, doing thus a very radical removal but leaving a safe segment of thyroid tissue over the parathyroids and recurrent laryngeal nerves. When the trachea is bared and only the segments *c* left, then the shaded and dotted area *b* represents the extra amounts of thyroid tissue which can be removed with this procedure as opposed to leaving a segment of tissue over the trachea.

We have, in addition to removal of the isthmus, carefully searched in all cases for pyramidal lobes, and in a very considerable number of cases found them extending up to the hyoid bone and amounting to good-sized segments of thyroid tissue.

If one will look at the diagram, Fig. 7, it will be evident that if a section of thyroid is to be left over the trachea, then larger segments of thyroid tissue must be left on either side, and that only by complete removal of the isthmus is it possible to extend the resections laterally into the bodies of the thyroid lobes.

When the isthmus is removed, one may remove with it, as shown in Fig. 7, good-sized segments of the lateral lobes and still leave safe remnants of thyroid tissue over the regions of the parathyroid bodies and the recurrent laryngeal nerves. (Figs. 8, 9, 10.) This technical step is, we believe from our experience with it, an important feature in one's ability to remove in primary hyperthyroidism sufficient thyroid tissue to bring about a cure, but still to leave enough over the danger areas to prevent injury to the parathyroid bodies and the recurrent laryngeal nerves.

CONCLUSIONS.—Due to the needs for thyroid secretion in development,

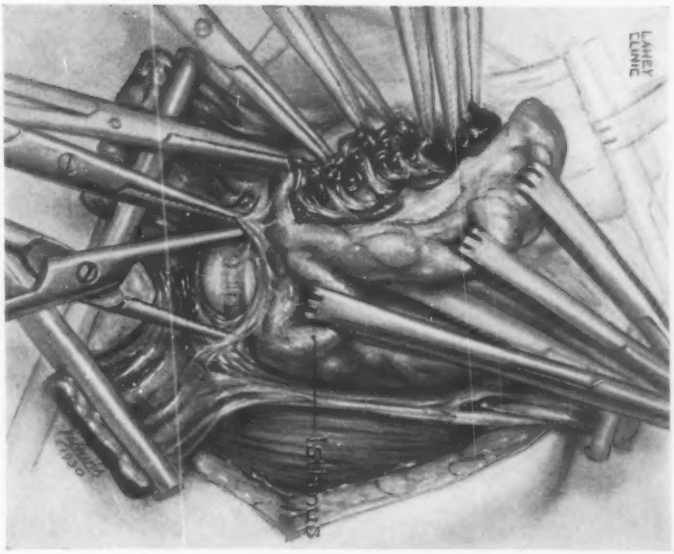

FIG. 8.—Showing the lateral lobe of the thyroid inverted, turned inward and the posterior segment which is to be left behind marked out with snaps and cut. The isthmus has been grasped, turned up and is being separated from the trachea by a hæmostat. (Surgical Clinics North America. W. B. Saunders Co.)

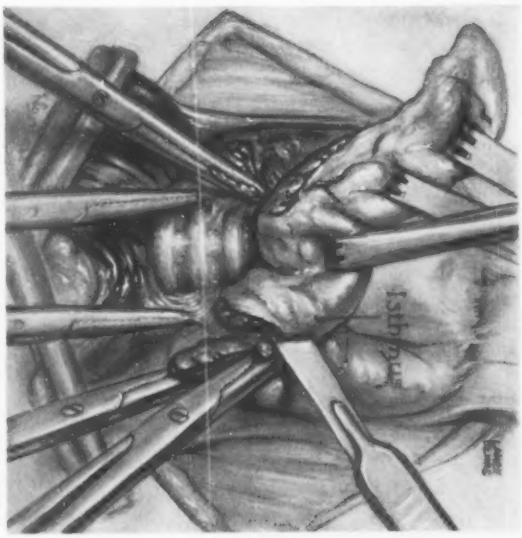

FIG. 9.—Showing the isthmus separated and turned up from the bared trachea. The attachment of the isthmus to the remaining lobe is being cut away. Note the complete removal of the isthmus and complete baring of the trachea. (Surgical Clinics North America. W. B. Saunders Co.)

care must be exercised in thyroidectomy for hyperthyroidism in children that too much thyroid tissue is not removed and myxœdema produced.

Due to the relative inactivity of the thyroid in elderly patients, care must be exercised lest radical thyroidectomy produce a high percentage of myxœdema in such patients.

Good-sized remnants of thyroid tissue must be left after subtotal thyroidectomy, when, following the pre-operative administration of iodine, marked involution of the gland has occurred.

Radical removals of thyroid tissue must be done and but small remnants left in patients with uninvoluted thyroids, if one wishes to produce cures in patients with this type of uninvoluted thyroid gland.

Clinical features indicating the presence or absence of involution are mentioned.

Good-sized remnants of thyroid tissue must be left in subtotal thyroidec-

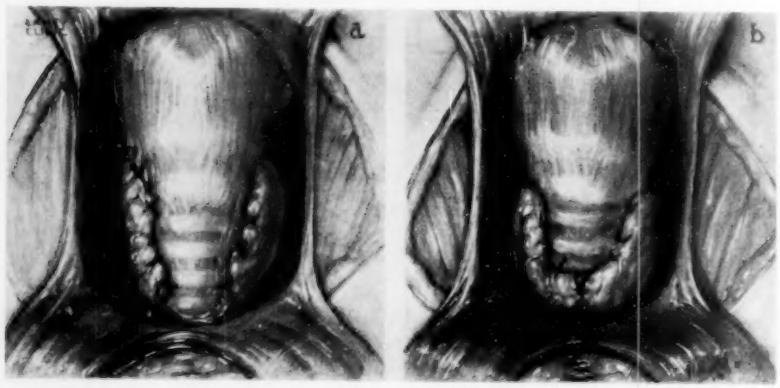

FIG. 10.—(*a*)—Showing the remnants of the thyroid left on either side of the trachea with the isthmus completely removed and the trachea bare. Note the remnants of the thyroid turned inward and sutured against the trachea so that all raw surfaces are faced against the trachea. (*b*)—The lower segments of the thyroid remnants can often be sutured together across the trachea to form a new isthmus and thus restore symmetry in the feminine neck after radical subtotal thyroidectomy. (Surgical Clinics North America. W. B. Saunders Co.)

tomy for hyperthyroidism associated with hyperinvolution or multiple colloid adenomatous goitre.

Complete removal of the isthmus of the thyroid and baring of the trachea do not produce any disturbing amount of post-operative tracheitis. Attempts to leave segments of the thyroid isthmus over the trachea make one tend to leave too large remnants of thyroid tissue, particularly in primary hyperthyroidism. Complete removal of the thyroid isthmus with premeditated baring of the trachea and with extensive removal of thyroid tissue from the lateral lobes of the thyroid leaves a safe amount of thyroid tissue over the recurrent laryngeal nerve and the parathyroid bodies, and makes possible the radical removals of thyroid tissue which are often necessary to bring about lasting cures in hyperthyroidism.

THYROID CRISIS

By Earle I. Greene, M.D.

associate in surgery, northwestern university medical school

and

J. Major Greene, M.D.

clinical assistant in medicine, rush medical college

of Chicago, Ill.

One of the most serious complications associated with the hyperthyroid state is the condition known as thyroid crisis, or, as is described by others, thyroid storms, acute hyperthyroidism, thyroid delirium, or acute thyroidism. That it carries a most substantial risk can best be attested to by the remarks of Lahey[1] when he tells us that in 1927 there were 1,118 operations for thyroid disorders at the Lahey Clinic with six deaths. During this corresponding period there was an equal number of deaths as a result of acute thyroid crisis—as many patients dying from the acute hyperthyroid state as died from 1,118 operations on the thyroid gland.

According to most authorities, the acute thyroid crisis is peculiar to the exophthalmic goitre, and apparently does not occur in the adenomatous goitre with hyperthyroidism unless there is some associated parenchymatous hypertrophy in the remaining gland. It is a well-known fact that the course of exophthalmic goitre is characterized by incomplete remissions and exacerbations, and it is during such periods that the condition of crisis is so prone to occur. In our series, however, we have one case in which a large adenomatous goitre was removed at operation, no hyperplastic tissue being found.

Thyroid crisis may occur in individuals in whom there is no suspicion of thyrotoxicosis as described recently by Dixon, and Judd and Dixon. It most frequently occurs, however, in patients known to have hyperthyroidism. It may appear without any apparent inciting cause, or may come as the result of an apparent trifling incident which ordinarily would make no impression on the normal individual. It may appear immediately after operation or several days after surgical intervention.

The majority of crisis cases occur in patients in whom the hyperthyroidism has been present for some time. Either these patients have not sought relief from their hyperthyroidism or they have had only half-hearted treatment on the part of their attending physicians. Hyperthyroidism must not be permitted to go on. Treatment must not be delayed, and if we are to eradicate hyperthyroidism as well as all the complications resulting from hyperthyroidism, our treatment must not be one of watchful waiting. If we are to prevent irreparable myocardial injury, irremedial parenchymatous injury, acute hyperthyroidism with its attendant high mortality, if we are to do away with persistent exophthalmos, we must not procrastinate and treat

our patients with iodine, thyroidectin, digitalis, X-ray, radium, or ultra-violet ray, but must insist on proper surgical intervention as soon as the patient is adequately prepared.

Acute hyperthyroidism is frequently ushered in by physical fatigue, by intense psychical stimulation such as fright, anger, or sorrow, by an intercurrent infection such as an acute tonsillitis, acute sinusitis, acute appendicitis or an acute cholecystitis. It may follow a serious emotional stimulation such as a death in the family, the witnessing of a gruesome accident, or it may come on after a minor surgical procedure such as the opening of an infected finger, the opening of an abscess, or injection of a varicose vein.

Unrecognized, potential or latent hyperthyroidism has long been known. It is in these patients that death may be the result following some operative procedure, unless the condition is recognized and proper therapy instituted without delay. Dixon recently reports such a case occurring in a young woman who complained of pain in the right lower quadrant. While being observed in the hospital she had an acute attack, and at operation an inflamed appendix was removed. The immediate post-operative period was without incident, the temperature remaining between 99° and 100°. Without apparent cause the temperature rose to 104.2°, the pulse, which was 80, rose to 160 per minute, and a distinct tremor was noted. Peritonitis, hæmorrhage, and other post-operative complications were ruled out and a diagnosis of impending thyroid crisis was made. Under large doses of compound solution of iodine the entire picture was changed after twenty-four hours. A characteristic exophthalmic goitre was later removed. Had this condition been unrecognized it is safe to say that she probably would have gone into a serious condition. Here we see a case of latent hyperthyroidism which became manifest following the shock of a surgical procedure.

Every hyperthyroid patient is a poor risk when any form of treatment not aimed to relieve the hyperthyroidism is instituted. No evident hyperthyroid patient should be exposed to tonsillectomy until after the thyrotoxicosis has been controlled, or a serious crisis may be the result.

Some years ago one of my colleagues had such an unfortunate case. His patient, a mild case of hyperthyroidism, was referred to him for tonsillectomy because of recurrent attacks of tonsillitis. The attending physician felt that if all foci of infection were eradicated, the thyroidism might be more easily controlled. The operation was a simple procedure, but almost immediately vomiting set in. The pulse became very rapid and diarrhœa very distressing. The patient lapsed into a deep coma, dying in an acute thyroid crisis.

Recently we observed a fatal case of thyroid crisis following the injection of a varicose vein. The patient was markedly hyperthyroid; he also had varicose veins and one varicose ulcer which distressed him greatly. Injection of the veins was refused until after the hyperthyroidism was controlled. The veins in the region of his painful ulcer, however, were injected by another physician. Evidently there was considerable extravasation of the injected

material, for he complained of severe pain at the site of injection, and within a short period of time was in a severe crisis. Heroic treatment was instituted but to no avail.

Procedures which are life-saving in character, however, such as an operation for an acute appendix, must not be postponed, but the patient should be fortified as best he can, immediately before and after the operation, to prevent a fulminating hyperthyroidism. In short, any measure unless life-saving in character not aimed at relieving the hyperthyroidism should best be postponed until after thyroidectomy has been performed.

The incidence of thyroid crisis is extremely low, the average man seeing few, if any, in his life's work. It must be said, however, that prior to the use of iodine in the treatment of hyperthyroidism, cases of crisis before and especially after operation were more common. In justification to the average man it is only fair to say that he is recognizing hyperthyroidism earlier and sending them to the surgeon sooner, thus preventing the serious thyroid crisis as well as the other complications peculiar to this disease.

Before the days of adequate pre-operative preparation of the patient with iodine, post-operative thyroid crisis was not infrequent. Fortunately, the use of iodine has revolutionized the entire aspect of the surgical treatment of thyrotoxicosis. Where three or four operative procedures (bilateral polar ligations, and two-stage thyroidectomy) were resorted to, frequently attended with severe reactions following each procedure, today by far the greatest per cent. of cases are completed in one stage, with post-operative reactions reduced to a minimum. Although uncommon, we must not lose sight of the fact that they occur even today and we must be prepared to recognize this condition immediately and institute judicious treatment before the patient becomes serious.

Adequate pre-operative preparation with iodine will in the majority of cases prevent post-operative acute hyperthyroidism. It is a dangerous procedure to put every patient on thirty minims of Lugol's solution daily and feel that the patient is safe against severe reactions. It is likewise unsafe to rely on a single low metabolic rate, for, indeed, we have often seen highly toxic patients with comparatively low basal rates. Conversely, we have met with patients who, in spite of marked clinical improvement under Lugol's solution, have had a rise in their basal rate. It is only through experience and judgment that the optimum time for operation is best ascertained. If we must lay down rules, the following should be fulfilled: (1) The weight curve must be on the upward rise; (2) the pulse must nearly approximate, or be within, the normal range; (3) nervousness, apprehension and emotional instability must be adequately controlled; (4) a falling metabolic rate, preferably below +20. The fulfilling of these criteria would constitute the ideal surgical risk, which, however, is only occasionally met. We not infrequently operate on patients with basal rates of over +35, with pulses over 90, but

whose general condition is, nevertheless, sufficiently good to warrant doing a thyroidectomy.

The picture of crisis may appear suddenly with extreme violence, or come on gradually with definite premonitory symptoms. As a rule, crisis cases occurring without any definite precipitating factors first show evidence of increasing toxicity, such as a rising pulse, increased excitability and lessened emotional control. Injury, infection, an operation, a death in the family, or a severe fright occurring in a hyperthyroid individual may cause an acute crisis with little or no warning. Post-operatively, the picture of crisis may appear immediately or as long as forty-eight to seventy-six hours.

The actual crisis usually manifests itself by an attack of vomiting and diarrhœa, which soon becomes distressing. The pulse climbs rapidly and steadily, often becoming uncountable. The temperature rises to from 104° to 107°, although exceptional cases have been known in which the temperature remained normal. Restlessness becomes extreme so that the patient is held in bed with considerable effort, often requiring mechanical restraints. The face becomes flushed, and sweating profuse. Talkativeness merges into delirium and may be followed by coma, from which the patient can be aroused only with difficulty. If this condition is permitted to continue, the vomiting and diarrhœa become less frequent. As dehydration occurs, the skin and mucous membranes become extremely dry. The pulse continues to rise and auricular fibrillation may set in with a marked pulse deficit. The final picture is one of profound coma terminating in death.

The exact mechanism by which a crisis might be set in motion is not known. Goetsch makes the suggestion that in hyperthyroidism there is an extreme sensitiveness to adrenalin. Crile makes the suggestion that thyroxin sensitizes the tissues to adrenalin. He says: "Adrenalism increases hyperthyroidism, hyperthyroidism increases adrenalism (*i.e.*) hyperthyroidism and adrenalism co-exist, each augmenting the other." Thus a vicious circle is created. Excessive handling of the hyperplastic tissue at operation, liberating relatively large amounts of thyroxin into the blood-stream, has been suggested to explain post-operative crisis, but, indeed, we have seen cases in which there has been a minimum of handling yet the acute manifestations have occurred. It must be said, however, that a properly prepared patient, a careful rapid one-stage thyroidectomy, and adequate post-operative therapy consisting of iodine from 50 to 120 minims during the first twenty-four hours, plenty of fluids given by mouth, rectum, or, if necessary, subcutaneously or intravenously, plenty of sedatives for the first twenty-four to forty-eight hours, will tend, in the majority of cases, to prevent severe reactions.

Thyroid crisis is a grave emergency. The patient with an impending thyroid crisis, or one already in an active crisis, can well be compared to the patient in an impending or already in a diabetic coma, and if the patient is to remain alive, treatment, often heroic in character, must immediately be insti-

tuted. Lahey says: "Just as there is an emergency treatment for impending diabetic coma, there should be and is an emergency treatment for the impending thyroid crisis."

Our armamentarium in this condition consists for the most part of iodine, fluids, glucose, and morphine. Our success with this treatment must depend, however, upon the early recognition of the condition. If applied early and in sufficient amounts before full development of the crisis, a happy outcome will be the result in the majority of cases. Recognized late, when the patient is in an active crisis, the results are often most disappointing.

We have seen patients change, within twenty-four hours, from critically ill individuals, semi-comatose with diarrhœa, vomiting and high temperature, to moderately hyperthyroid patients after the administration of 120 minims of compound solution of iodine. Iodine is by far the most valuable and most effective measure we have at our command. One further statement regarding iodine in this connection must be made. It is a well-known fact that once a patient has improved under iodine therapy, it seldom can be repeated with the same degree of efficiency, unless the iodine has been withdrawn for a long period. Even after withholding iodine for a considerable period, it is doubtful whether the same striking benefit can again be obtained when it is resumed. Since every hyperthyroid patient is a potential crisis case, are we not robbing such a patient of perhaps a life-saving measure in the event a crisis occurs by continuing iodine over a long period of time instead of using it as a measure preparatory for operation?

Just how we will administer the iodine will depend upon the patient's condition. If the state of affairs is recognized early, before the onset of vomiting, iodine may be given by mouth, in doses of twenty to thirty minims, every three or four hours until 100 to 150 minims are given, or until a decided clinical improvement has occurred. Should there be vomiting without diarrhœa, Lugol's solution can be given by rectum. If vomiting and diarrhœa are both present, then we must resort to either the intravenous route, or give it under the skin. By hypodermoclysis from thirty to fifty minims of Lugol's solution may be given in 1,000 to 1,500 cubic centimetres of saline solution and repeated when necessary. Should the intravenous route be found necessary, 0.5 gram (7.5 grains) of sodium iodide may be given together with saline or saline and glucose. In the semi-comatose patient iodine may be given by stomach tube and repeated as often as necessary.

In addition to iodine these patients must have sufficient fluids and fuel. Because of the vomiting, diarrhœa, profuse sweating and the curtailment of fluids dehydration becomes a serious factor and must be replenished if the toxæmia is to be combated. Because of the rapid burning of glycogen in hyperthyroidism, but most especially in the crisis, there is a depletion of the glycogen reserve of the body which must be replaced. From 75 to 100 grams of glucose in 1,000 cubic centimetres of normal salt are given into the blood-stream very slowly, and repeated every five or six hours until the general condition has decidedly improved.

Because of the extreme restlessness sedatives must be given and repeated as often as necessary. Hyperthyroid patients need larger doses of morphine than do other acutely ill patients, and should be given in quarter-grain doses repeated as often as is necessary. Paraldehyde and sodium amytal given intravenously have been suggested as means of controlling the restlessness.

Ice packs have been advocated when the temperature reaches 103° and are said to relieve restlessness, lower the temperature and pulse, and induce sleep.

Operative procedures upon patients who have recovered from a crisis must be done with extreme caution. Some goitre surgeons feel that such patients can be adequately prepared within a short period of time. These patients have passed through a profound shock and stand surgery poorly. They can well be compared to a badly injured individual in shock, and no surgeon would attempt any radical procedure until the shock is adequately controlled. Instead of the ten days' preparation following a crisis, as is advocated by some goitre surgeons, we feel that such patients must have a much longer period of preparedness, as long as three to six weeks after the acute phase has passed, and, if necessary, longer. Then we can safely do a one-stage operation with comparative ease and safety.

Summary.—(1) Thyroid crisis is one of the most serious complications of hyperthyroidism.

(2) As a rule this condition occurs in the primary toxic, or exophthalmic goitre.

(3) Thyroid crisis usually occurs in patients known to have hyperthyroidism but in whom no treatment has been sought or in whom inadequate treatment has been instituted.

(4) Thyroid crisis may occur in individuals in whom there is no suspicion of thyrotoxicosis.

(5) A crisis may come on immediately after operation or several days later.

(6) Acute hyperthyroidism may be ushered in by physical fatigue, by psychical stimulation, as a result of an intercurrent infection or appear after some surgical condition often trivial.

(7) Measures not aimed to relieve the hyperthyroidism should be postponed until after thyroidectomy has been performed.

(8) Adequate pre-operative therapy will in the majority of cases prevent post-operative acute thyroidism.

(9) The picture of crisis may appear suddenly with no premonitory manifestations, or make its appearance slowly with definite symptoms.

(10) The mechanism whereby a crisis is set into motion is not known.

(11) The condition must be recognized early and proper therapy instituted immediately or death will frequently result.

(12) Treatment consists of iodine, fluids, glucose, and morphine.

(13) After recovery from a crisis, surgical intervention should be done with caution waiting sufficiently long enough to get the patient in proper physical condition.

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MALIGNANT TUMORS AND TUMOR-LIKE GROWTHS OF THE THYMIC REGION

By Douglas Symmers, M.D.

of New York, N. Y.

FROM THE PATHOLOGICAL LABORATORIES OF BELLEVUE HOSPITAL

In the Pathological Laboratories of Bellevue Hospital, I have had occasion to study a series of twenty-five malignant tumors or tumor-like growths of the thymic region occurring among approximately 17,000 autopsies, an incidence of 0.14 per cent. This, I believe, is the only large group of cases of this sort to be recorded by a single observer, the literature consisting practically exclusively of scattered contributions. Of the latter, Rubaschow[1] collected a series of forty-four examples of sarcoma, thirty-three of which were described as of the lymphocytic type, together with five cases which were designated either as epithelioma or as "cancer medullare." The twenty-five growths studied at Bellevue Hospital were interpreted as originating in the thymus or its remains—a conception based on the fact that all of them occupied the position normally assigned to the thymus; that all of them were solid growths; that all of them presented a histology in keeping with tumors arising from the several types of tissue that enter into the structure of the thymus; that in all of them no growth was encountered in any other part of the body that could be construed as primary; that all of them pursued a noticeably similar scheme of invasion and destruction of adjacent tissues; that many of them feigned the shape of the thymus, including the presence of a notch at its lower or pericardial end; and, finally, that no more logical source of origin could be determined among the contents of the anterior mediastinum than that of the thymus or its débris.

Of the twenty-five Bellevue Hospital cases, eight were of the group of the so-called peritheliomata, nine were lymphosarcomata, five were examples of Hodgkin's disease, two were epitheliomata and one was a spindle-cell sarcoma arising, most probably, from the connective-tissue framework of the thymus. In this paper I have followed the older nomenclature of tumors, bad as it is. By usage it has acquired meaning. I have avoided the newer designations, such, for example, as "thymoma," as the further inappropriate use of language. "Thymoma" means "tumor of the thymus," using the word, tumor, in the sense of an autonomous new growth and not merely as a swelling. Any tumor of the thymus, it follows, is a "thymoma"—whether it be epithelioma, spindle-cell sarcoma, lymphosarcoma, perithelioma, or whatnot. "Thymoma" is oftenest applied, however, to lymphosarcoma of the thymus. The discrimination is obviously misleading, since the designation in question does not provide for the inclusion of tumors of the thymus other than lymphosarcomata. It is difficult to understand why one should use "thymoma" as a designation for lymphosarcoma of the thymus, while retain-

ing the appellation "lymphosarcoma" for tumors of identical nature in other parts of the body. As yet, so far as I am aware, no such word as "intestinoma" has been coined for lymphosarcoma of the intestine, nor "gastrinoma" for lymphosarcoma of the stomach. The practice of naming tumors after the organs in which they arise is a philologic desecration. Thus, "hypernephroma" is meaningless except as the designation for a tumor somewhere "above" the kidney. "Thymoma," therefore, is a variety of hypernephroma, since the thymus, in the animal of erect posture, is "above" the kidney—a *reductio ad absurdum*. "Hepatoma" conveys no conception of the cell derivation of the several tumors of the liver. "Ovarioma" does not serve to clarify our knowledge of the cell origin of tumors of the ovary. And so on through that gamut of neoplasms where the suffix, *oma*, is arbitrarily attached to the name of a viscus to indicate the origin in it of a particular variety of new growth irrespective of the patronymic rights of other tumors of different cell genesis arising in the same organ.

For purposes of this presentation, the Bellevue Hospital cases have been assembled in such manner as to attempt the portrayal of thymic tumors or tumor-like formations as a composite which, although made up of lesions of divergent histology, is nevertheless attended by methods of growth behavior that are often strikingly alike. Thymic lesions of the sort here described are susceptible of diagnosis during life, although, as a rule, only late in their course. Even in these circumstances appropriate treatment, such as X-ray therapy, may mitigate the symptoms incident to increased intrathoracic pressure. In others it may provide alleviation over such an extended period as to constitute what is familiarly characterized as a clinical cure. With the advance of thoracic surgery, it is conceivable that some of the tumors under discussion might be approached from the operative standpoint, since wider knowledge of their existence may lead to the application of diagnostic methods aimed at their earlier detection. In any event, an understanding of the diversified pathology of thymic growths assists one to apply with greater assurance those remedial measures which are known to afford relief in certain forms of growth and, conversely, more intelligently to appraise the reactions of a patient under treatment for a type of growth that is known successfully to resist all methods of therapeutic restraint. In the first group I refer particularly to the lymphosarcomata and Hodgkin's disease, in the treatment of which mitigation of the distressful symptoms of increased intrathoracic pressure is not uncommonly achieved. In the second group I refer to such growths as the epitheliomata, where the outlook is not any too hopeful, and to such ruthless tumors as the peritheliomata, where treatment as now practiced is futile.

In order to formulate an intelligent conception of the origin and behavior of malignant tumors and tumor-like growths of the thymus and its remains, it is necessary to appreciate certain fundamental facts having to do with the embryogenesis and histologic structure of the thymus itself. Investigators are agreed that Hassall's corpuscles and the reticulum cells from

which they spring are of epithelial origin. The derivation of the chief elements of the organ, namely, the small cells, has been the subject of debate. Maximow[2] believed that, early in the process of development, the thymus is invaded by mesenchymal elements which differentiate into lymphocytes and that these accumulate in such numbers as to lend to the organ the appearance of a lymphocytic structure. Maximow's belief in the lymphocytic nature of the small cells is opposed by Stöhr[3] and others, but is shared by Hammar,[4] Schaffer[5] and Pappenheimer.[6] The latter has described, in the small cells of the thymus, granulæ which are identical with those in the lymphocytes of the blood. As a corollary, he has demonstrated that in clotted plasma cultures there is a difference in the behavior of the two types of cells in the thymus—

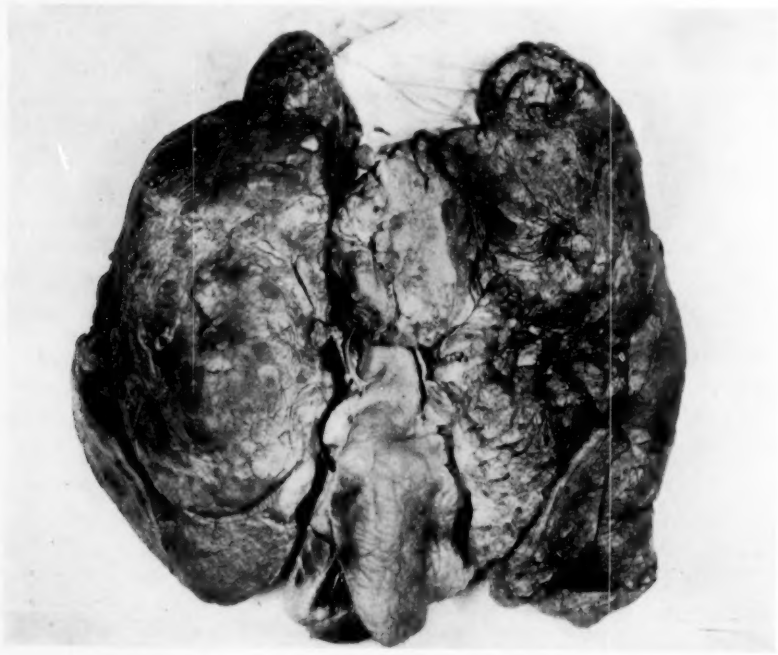

FIG. 1.—Epithelioma of thymus, showing infiltration of anterior margin of left lung. This is the same growth which is shown photomicrographically in Figs. 3 and 4.

a fact which militates against the acceptance of the view that both of them are of epithelial origin. Furthermore, the conception of the small thymic cell as a lymphocyte is in consonance with our knowledge of the pathology of the thymus, especially of certain tumors which spring from it or from its remains, notably the lymphosarcomata. In addition, the histology of the fully developed thymus affords evidence, not only that its origin is to be traced to two separate sources, but that it is related to the lymph-nodes. Thus, the cortex of the thymus is composed of densely packed cells which are structurally identical with the lymphoid elements of the lymph-nodes and with the cells of the lymphoid follicles in the spleen, the individual cell collections in the cortex being separated from one another by a system of

vascularized connective-tissue septa. In the medulla the same small cells are present, but are more loosely packed and occur in lesser numbers, while in the midst of them and standing out in contrast are the relatively large epithelial whorls known as Hassall's corpuscles, together with a delicate epithelial reticulum.

From each of the histologic structures enumerated, a particular sort of malignant tumor is capable of arising—epithelioma from the epithelial reticulum and Hassall's corpuscles; lymphosarcoma from the lymphocytic elements; from the blood-vessels that variety of malignant growth known as perithelioma or as perithelial sarcoma, the histologic unit of which is a small vessel surrounded by a mantle of tumor cells, the latter probably springing from the connective tissue of the vascular wall, and spindle-cell sarcoma from the supporting connective tissue. Finally, since the thymus is a constituent of the lymphoid system, it is not surprising to find that its residua are capable of those transformations which constitute Hodgkin's disease.

THE PERITHELIOMATA

CASE I.—Male, aged fifty, admitted March 1, 1927; died March 5, 1927. Two months before admission, the patient stated, he had "caught cold," followed by persistent cough, which was made worse by lying down, and by spitting of blood. He complained also of precordial pain, palpitation of the heart on exertion, and of dyspnœa amounting finally to orthopnœa. At the time of admission the patient was cyanotic; breathing was rapid and forced; the superficial veins over the upper chest wall, both in front and behind, were greatly dilated. Physical examination revealed a hard swelling above the right clavicle. Percussion showed marked dullness over the manubrium and to the right as low as the level of the second rib. Fluoroscopic examination revealed a large mass in the upper and anterior mediastinum. Death occurred about nine weeks after the onset of symptoms.

Autopsy.—On opening the chest, an enormous tumor came into view occupying the position of the thymus gland. The tumor, which was about the size of a grapefruit, was closely adherent to all the structures at the base of the heart and extended into the neck as far as the thyroid gland, which it invaded. On the right side it infiltrated and replaced practically the whole of the upper lobe of the right lung; in a downward direction it penetrated directly into the pericardial sac. The aorta and pulmonary artery were almost entirely surrounded. The right bronchus was completely enclosed and its lumen was greatly narrowed. The surface of the right kidney was studded with small, white plaques which varied in size from 2 to 5 millimetres. On section, these extended through the cortex into the medulla. Both adrenals were markedly enlarged and infiltrated by tumor growth.

Histology.—Microscopic examination shows the presence of a richly cellular tumor made up of a ground-work of rather poorly vascularized fibrous connective tissue, imbedded in which are islands of small, richly chromatic, spindle-shaped tumor cells arranged sometimes in long, slit-like apertures, but oftenest in the form of rounded or oval or elongated islands of different sizes. Throughout the tumor are numerous congregations of spindle-shaped cells arranged radiately to the walls of small blood-vessels. These radiate cell formations soon lose their individuality, however, and grow diffusely as collections of spindle-shaped cells with no definite arrangement.

CASE II.—Male, aged fifty-five, admitted June 23, 1925; died July 13, 1925. Four months before admission, the patient suffered an attack of "grippe" followed by persistent cough and spitting of blood, amounting sometimes to a half-pint. During the

three weeks previous to admission, he became increasingly short of breath on exertion and could not walk up one flight of stairs without resting; he also complained of difficulty in swallowing. On admission, fluoroscopic examination showed a non-pulsating mass in the anterior and upper mediastinum. The heart and trachea were displaced to the left. Death occurred four months and three weeks after the onset of symptoms.

Autopsy.—In the upper and anterior mediastinum was a large tumor which surrounded and was closely adherent to the œsophagus, trachea, the main branches of the left bronchus, and the aorta. The growth invaded the œsophagus, forming a small,

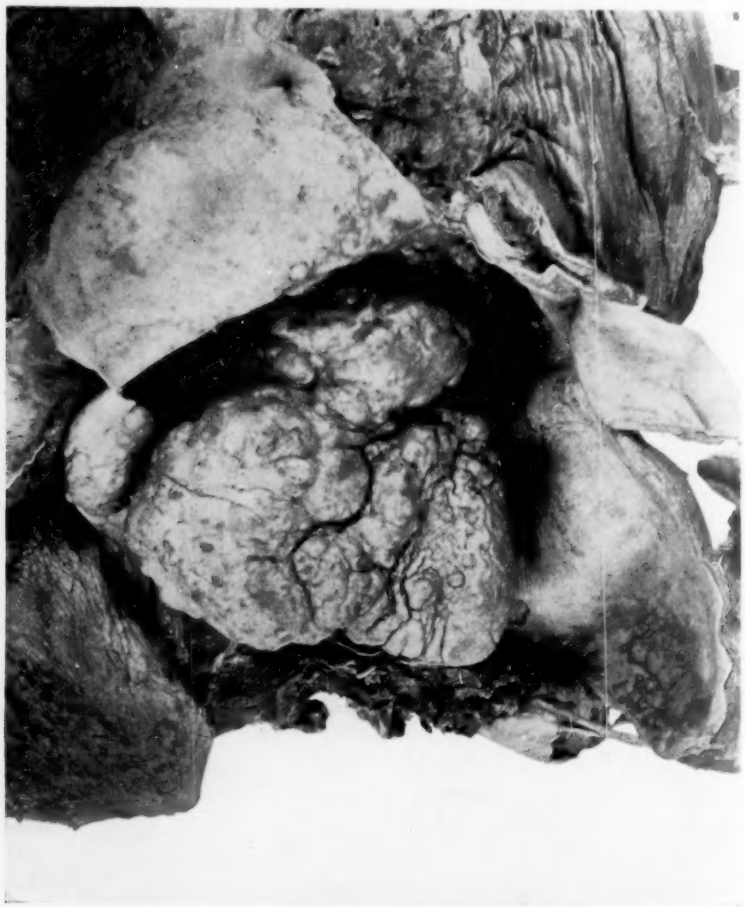

FIG. 2.—The heart and pericardium in a case of thymic Hodgkin's disease, showing almost complete nodular replacement of both auricles and of the upper portion of the right ventricle, together with infiltration of the parietal pericardium.

cauliflower-like projection into its lumen for a distance of about 5 centimetres. The tumor invaded the left main bronchus and several of the smaller bronchi and replaced the lower third of the left lung, which was firmly attached to the diaphragm below, the left chest wall laterally and posteriorly, and to the pericardium antero-medially. All the lymph-nodes at the hilus of the left lung were large and were replaced by grayish-white tumor tissue. Portions of the pleura, which were removed with the lower lobe of the left lung, were greatly thickened and presented much the same naked-eye appearances as that of the growth in the mediastinum. The liver was enlarged and studded with nodules which were sharply circumscribed, grayish-white in color,

some of them centrally softened. The largest of these nodules measured from 2 to 3 centimetres in diameter. A number of metastatic deposits were present throughout the mesentery, the larger ones measuring about ½ centimetre in diameter.

Histology.—At numerous intervals are collections of spindle-shaped tumor cells arranged radiately to the walls of small blood-vessels. The radiate formation is soon lost, however, and the spindle-shaped cells grow diffusely and arrange themselves in slit-like crevices or as islands of variable size and shape.

Case III.—Male, aged fifty-four, admitted November 6, 1929, died December 29, 1929. Three months before admission, the patient began to complain of shortness of breath amounting at times to orthopnœa and of difficulty in swallowing both solids and liquids. At about the same time his feet began to swell. The chest was tapped on three different occasions and a total of 4,500 cubic centimetres of fluid was withdrawn. On admission to Bellevue Hospital, the patient's face was cyanotic. The veins of the anterior chest wall were engorged and tortuous. The face and neck were

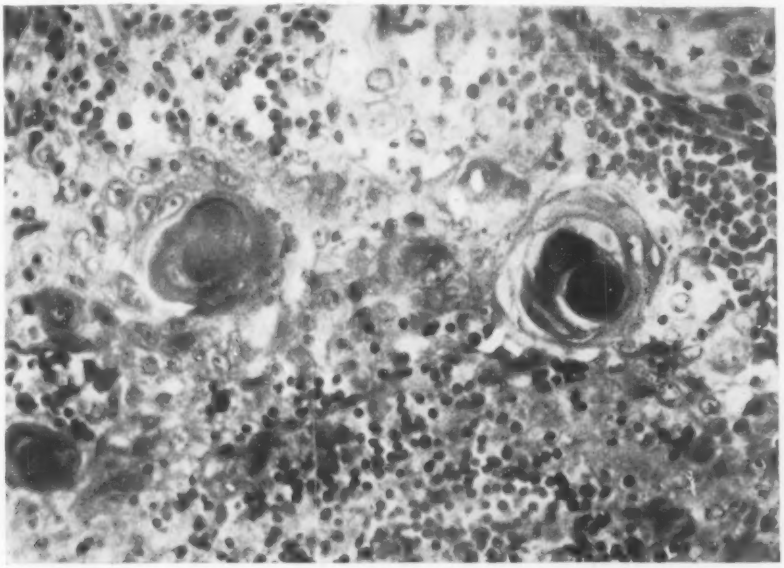

Fig. 3.—Epithelioma of the thymus, showing, in sections from the main growth, small numbers of lymphocytes among which are to be seen large, clear, sharply defined epithelial reticulum cells undergoing lamellation to form Hassall's corpuscles.

œdematous and the right side of the chest showed signs of fluid. The heart was displaced to the left. Thoracentesis was done on two occasions and released a total of 2,500 cubic centimetres of blood-stained fluid. The patient's condition became steadily worse; dyspnœa and cyanosis were more marked; he was unable to speak above a whisper; there was marked œdema of the face, arms and legs and recurring hydrothorax and ascites. Death occurred five months after the onset of pressure symptoms.

Autopsy.—On inspection, the body showed œdema of the face, neck and upper extremities, and the chest and arms presented large, distended, tortuous veins. On removing the sternum, a mass was present in the upper anterior mediastinum that feigned the shape of the thymus. The mass insinuated itself around the structures at the base of the heart and invaded the superior vena cava and the innominate and right jugular veins. It extended into the substance of the right lung beside the bronchus, pressing upon and occluding the smaller bronchi so that the lung tissue beyond was atelectatic. The right pleural cavity contained 2,900 cubic centimetres of blood-tinged

fluid. On opening the pericardium, about 1,500 cubic centimetres of blood-stained fluid were present. The mass invaded the pericardial sac in the region of the superior vena cava. The parietal pleura of the right chest was 0.3 centimetres in thickness and was of the consistence of leather. The visceral pleura was likewise directly invaded and thickened by the infiltration of tumor tissue. The left lobe of the thyroid was nodular and, on section, showed a sharply circumscribed, rounded deposit which measured 5.5 centimetres in length, 3.5 centimetres in breadth and 2.5 centimetres in thickness. The medulla of the right adrenal presented a nodule 2.5 centimetres in diameter.

Histology.—Microscopic examination shows a richly cellular tumor, the unit of which is a small blood-vessel arranged around which, radiately to the long axis, is a mantling of tumor cells, terminating suddenly in a broad area of necrosis. This formation is maintained throughout the greater part of the original growth and its metastatic deposits, but in other places the vascular unit is lost and the tumor grows as islands of spindle-shaped cells lying in a stroma of connective tissue.

CASE IV.—Male, aged fifty-three, admitted July 17, 1929; died September 16, 1929. Six months before admission, the patient began to suffer from a cough, which came on in spells and was sometimes accompanied by a sense of choking and occurred more frequently at night. On admission to the hospital, the patient was noticeably dyspnœic and suffered from frequent attacks of cough of the "brassy" type. The face was cyanotic and the superficial veins of both upper extremities and of the chest and abdomen were dilated. Several enlarged lymph-nodes were felt in the supraclavicular regions. The right chest showed signs of fluid and there was brawny œdema of the right arm. Shortly after admission, the right chest was tapped on three occasions, releasing a total of 2,800 cubic centimetres of slightly cloudy, yellowish fluid. Death occurred eight months after the onset of signs of intrathoracic pressure.

Autopsy.—On opening the chest, a large mass came into view in the superior and anterior mediastinum that encircled the great vessels at the base of the heart and the trachea, compressing the upper lobe of the right lung. The superior vena cava was almost completely occluded by compression from the tumor. The growth was roughly spherical in outline and measured 9 centimetres in diameter. It penetrated the lung in the line of the right main bronchus, which was narrowed to about one-third its normal diameter, the walls of the bronchus being infiltrated by tumor tissue. In the pancreas were a half-dozen nodular masses, the largest measuring about 4 centimetres in diameter.

Histology.—Microscopic examination shows the presence of a cellular tumor composed of a fibrous framework lying in which are innumerable large or small, oval or rounded islands of rightly chromatic spindle-shaped cells, most of which are growing diffusely, others arranged radiately to the long axis of the lumina of small blood-vessels.

CASE V.—Male, aged fifty-four, admitted July 29, 1929, died August 11, 1929. In June, 1928, the patient commenced to suffer from shortness of breath, which continued for a period of about one year and became gradually more troublesome. At the time of admission to the hospital, he complained of difficulty in breathing and of pain in the sacral region. Physical examination revealed orthopnœa; cyanosis of the face; dilatation of the superficial veins over the anterior thoracic and abdominal walls; the heart was displaced to the left; the right arm was œdematous; the liver was palpable 6 centimetres below the right costal margin and 9 centimetres below the xiphoid. Death occurred one year and six weeks after the onset of dyspnœa.

Autopsy.—The upper anterior mediastinum was completely replaced by a mass about the size of a small grapefruit. This mass extended superiorly to the suprasternal notch and inferiorly to the base of the heart where it penetrated the pericardium in its upper and posterior aspect in the form of a solitary nodule measuring 5 centimetres in diameter. On the right side the growth invaded and destroyed the anterior half of the upper lobe of the corresponding lung. On the left the mass was limited by the parietal pleura. Anteriorly it lay immediately beneath the sternum and ribs, to both

of which it was adherent. Posteriorly it insinuated itself around the structures at the base of the heart and attached itself to the trachea, which it compressed. The liver was extremely large, weighing 5,500 grams. It was riddled by nodules varying in size from a few millimetres to about 8 centimetres, many of them showing central umbilication. The liver pushed up the diaphragm on the right side and obliterated the lower portion of the corresponding pleural cavity, the upper portion having been similarly obliterated by compression and invasion of the upper lobe of the lung from the tumor in the thymic region. No lymph-node enlargements were observed in any part of the body. The body of the fourth lumbar vertebra was almost completely replaced by a large white tumor nodule which projected itself beneath but did not penetrate the overlying periosteum.

Histology.—Microscopic examination shows the presence of a growth made up of innumerable blood-vessels arranged radiately to the long axis of which are collections of small, densely chromatic, spindle-shaped cells. In other places the tumor cells

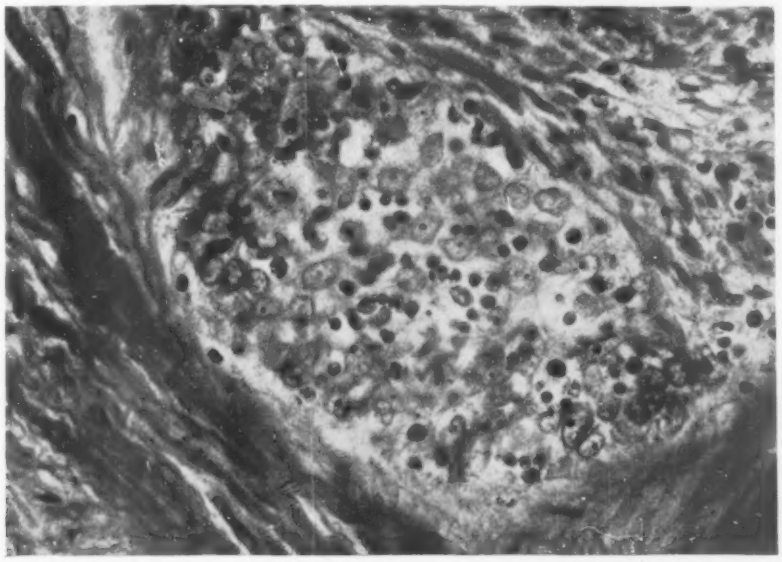

FIG. 4.—The same epithelioma as in Fig. 3, showing, in sections taken from the infiltrated lung, a few lymphocytes and considerable numbers of large, clear epithelial reticulum cells and absence of Hassall's corpuscles.

grow diffusely and are arranged in the form of large and small islands or as broad, intercommunicating, plexiform bands.

CASE VI.—Male, aged forty-one, admitted June 7, 1922, died September 14, 1922. The patient stated that, for a year before admission, he had suffered from a number of fainting spells preceded by pain beneath the sternum and palpitation of the heart. Otherwise there was nothing of interest in the clinical history, except for the fact that an X-ray picture, taken six months after the onset of symptoms, disclosed a new growth in the mediastinum.

Autopsy.—On lifting the sternum, an enormous mass came into view, occupying the anterior and superior mediastinum. The mass laterally was bounded by, but not attached to, the lungs. The upper end lay at the level of the suprasternal notch. The tumor was closely applied around the great vessels at the base of the heart, surrounding the aorta, the pulmonary artery, the great veins, the first part of the bronchi, and covering the anterior portion of the trachea. The growth extended downward over the upper half of the pericardium, which, however, it did not infiltrate. The lymph-nodes at the root of the lung were large, hard, and on section appeared to be infiltrated

by tumor growth. The right lung contained a deposit in the middle of the upper lobe that, on section, measured about 1½ centimetres in diameter. Above the pancreas was a soft, nodular mass which measured 7½ by 6 by 5 centimetres and consisted of fused lymph-nodes. These, on section, presented much the same naked-eye changes as that of the original tumor in the thymic region. The liver was greatly enlarged, weighing 5,525 grams. Throughout its substance were innumerable yellowish-white nodules, varying in size from ½ to 5 centimetres in diameter, many of them projecting above the surface.

Histology.—Microscopic examination shows a growth the unit of which is a blood-vessel surrounded by rather large, richly chromatic, spindle-shaped cells arranged radiately to the long axis of the vessel lumen and shading off into broad sheets of tumor cells in which few, if any, blood-vessels are visible.

CASE VII.—Male, aged fifty-one, admitted August 14, 1923, and died four days later. The patient's complaints at the time of admission were of œdema of the face, legs and hands, cough, shortness of breath, weakness, and rapid loss of weight. He stated that in the preceding three months he had had transient swelling of the face, legs and hands that had become persistent for the past month. Shortness of breath corresponded to these periods of œdema. He had had a cough for many years and this had become increasingly annoying with the advent of œdema. The patient finally became exceedingly weak and for this reason sought entrance to the hospital. Physical examination revealed, in addition to œdema of the face and extremities, that the respiratory movements were markedly diminished on the right side. Shortly after admission, the patient's right chest was tapped and 1,500 cubic centimetres of clear straw-colored fluid withdrawn. This was repeated two days later and 845 cubic centimetres were removed.

Autopsy.—The body was that of an emaciated male, showing œdema of both legs and of the right upper arm. On opening the chest, a massive whitish tumor came into view in the anterior and superior mediastinum that simulated the shape of the thymus. The growth extended upward into the root of the neck, especially on the right side, and downward to surround the bronchus of the right lung. The large vessels at the base of the heart were buried in the growth, but were not noticeably compressed. The pleura was studded with white nodules, varying in size from 2 millimetres to 5 centimetres, involving, especially, the dome of the diaphragm. In other places these nodules infiltrated the adjacent intercostal muscles. The pericardium was penetrated in its upper aspect and thickly infiltrated with tumor nodules derived directly from the mass in the anterior mediastinum. The lungs showed nothing worthy of note, except for the presence in the right lower lobe of a growth of tumor tissue extending along the walls of the bronchi and gradually thinning out towards the surface of the lung, spreading fan-fashion. The posterior mediastinal lymph-nodes were infiltrated, as were the nodes in the region of the pancreas, while the pancreas itself was occupied by nodular growths of the same type. The liver was enlarged and weighed 3,600 grams. It was diffusely studded with large reddish nodules, many of which were solid and elevated above the level of the capsule; others were umbilicated. The nodules measured on an average of about 3 to 5 centimetres in diameter and were well defined.

Histology.—Microscopic examination shows the presence of small blood-vessels, many of which are surrounded by a mantle of small, spindle-shaped, richly chromatic cells with scanty cytoplasm, the cells being arranged radiately to the long axis of the vessel. For the greater part, however, the tumor cells are laid down in a fibrous stroma as islands of various shapes and sizes, composed of cells of precisely the same type as those described.

CASE VIII.—Female, aged fifty-three, admitted September 23, 1929, died November 7, 1929. The patient stated that she had been in excellent health until six weeks before admission to the hospital, when she suddenly began to experience difficulty in swallowing. She was able to retain fluids until twelve days before admission, when vomiting

set in and was frequent. At about the same time she began to suffer from a sensation of choking, especially when lying down. Physical examination revealed continuation of cardiac dullness upward to the suprasternal notch and for a distance of about 2.5 centimetres on either side of the median line beneath the clavicles, together with an area of dullness in the corresponding interscapular region posteriorly. Death occurred three months after the onset of pressure symptoms within the thorax.

Autopsy.—On lifting the sternum, a mass came into view occupying the upper and anterior mediastinum that measured 10 centimetres in a downward direction and 7 centimetres laterally and simulated the shape of the thymus. The growth extended upward to the base of the neck and downward around the right bronchus and into the corresponding lung, the middle and lower lobes of which were collapsed and atelectatic. The mass was adherent to the aorta, the trachea and the upper end of the œsophagus.

Histology.—Microscopic examination shows moderate numbers of small vascular channels with a radiate arrangement of spindle-shaped tumor cells, the latter, at the extreme periphery, assuming a distribution circumferential to the lumen of the vessel. In sections taken directly from the tumor proper, atrophic but otherwise well-preserved Hassall's corpuscles were found in considerable numbers.

THE LYMPHOSARCOMATA

CASE IX.—Male, aged twenty-five, admitted April 9, 1914, died April 13, 1914. It was impossible to obtain a satisfactory history, but it was learned of him that, two and a half months before admission, a tumor-like mass appeared below the angle of the left jaw and a month later a similar mass became noticeable on the opposite side. Both gradually increased in size and the patient began to complain of difficulty in breathing that steadily increased. At the time of admission to the hospital, he presented marked orthopnœa and cyanosis of the face. Large, freely movable masses were present on both sides of the neck and the axillary and inguinal lymph-nodes were enlarged. The feet and legs were œdematous.

Autopsy.—The mediastinum, corresponding to the position normally occupied by the thymus, was filled by a huge tumor. The mass insinuated itself around the great vessels at the base of the heart and posteriorly to include the œsophagus, trachea and bronchi. The upper portion of the œsophagus was compressed and irregularly infiltrated by tumor tissue. The left primary bronchus was similarly infiltrated and almost completely occluded. Likewise, the walls of the superior vena cava were invaded. The growth penetrated the pericardium and both auricles and infiltrated the epicardial fat over the right ventricle. The right tonsil was enlarged to the extent of about 3 centimetres and, beneath the ramus of the left jaw, there was a solitary lymph-node likewise measuring about 3 centimetres in length. Otherwise the cervical nodes were free, as were the inguinal, femoral, retroperitoneal and iliac nodes. The nodes around the pancreas were enlarged to an enormous extent and the pancreas itself was diffusely infiltrated by whitish tumor tissue. In the wall of the small intestine were several nodules which measured about 3 centimetres in diameter. In the lower pole of the right kidney was a nodule measuring 1.5 centimetres in diameter.

Histology.—Microscopic examination of sections from the growth in the thymic region and from the enlarged lymph-nodes shows a rich aggregation of lymphocytes supported in a moderately cellular framework of connective tissue. Identical foci are found in the heart muscle, kidney, pancreas and the wall of the gut.

CASE X.—The patient, male, aged twenty-six, was admitted complaining that, three weeks before admission, he suddenly experienced difficulty in breathing and became subject to severe cough. Physical examination revealed, in addition to dyspnœa, cyanosis of the finger-tips, œdema of the subcutaneous tissues, and ascites.

Autopsy.—The subcutaneous tissues were universally œdematous. On lifting the sternum, the anterior mediastinum was found to be occupied by a growth which meas-

ured 9 by 13 by 10 centimetres and which conformed in a general way to the shape of the thymus. The tumor extended downward to the level of the auriculo-ventricular groove and upward to within a short distance of the lower border of the thyroid gland. Laterally it infringed on the root of the left lung and bands of tumor tissue extended along the connective-tissue planes around the larger bronchi for a distance of several centimetres. The substernal, peribronchial, peritracheal and lower cervical nodes were enlarged, discrete, the largest approximating the size of a cherry. The pericardium contained about 200 cubic centimetres of turbid fluid with fibrin flocculi, and both layers were covered with fibrinous exudate. The epicardial fat was diffusely infiltrated by grayish-yellow tissue, similar to that of the growth in the region of the thymus. The walls of both ventricles were enormously thickened and rigid, and were largely replaced by grayish-yellow tumor tissue, only islands of reddish musculature showing through at intervals. The parietal and diaphragmatic pleuræ on the right side measured 0.5 centimetre in thickness and were adherent to the chest wall, pericardium and diaphragm through the medium of infiltrating tumor tissue. The kidneys were

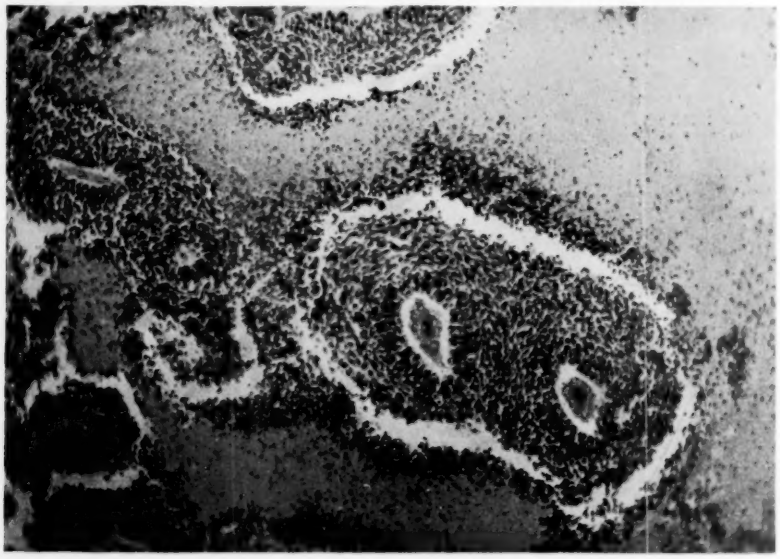

FIG. 5.—Low-power photomicrograph from a perithelioma of the thymus, showing the vascular unit of growth with its radiate and circumferential arrangement of spindle-shaped tumor cells, together with peripheral zones of necrosis.

massively enlarged and weighed, together, 1,300 grams. Each measured 17 by 8.5 by 8 centimetres. The cortices were unusually broad and grayish in color, standing out in contrast to the dark red pyramids.

Histology.—Microscopic examination of sections from the mass in the thymic region reveals a markedly cellular growth composed of lymphocytes, the cells in places being closely packed, in other places grouped in islands of various sizes, in still other places presenting a streak-like alignment. In the lymph-nodes the cellular unit is morphologically identical with that in the thymic growth, but the distribution of the cells is diffuse rather than insular or striate. In the heart muscle, incursion of lymphocytes occurs to an amazing extent, almost every individual muscle fibre being separated from its fellow by a dense infiltrate of lymphocytes, the muscle fibres compressed and their striations lost. Sections from the kidney disclose interstitial invasion by lymphocytes in proportions no less prodigious than those encountered in the heart, the infiltration extending from pelvis to cortex, bringing about wide separation of the tubules. Except

for minute interstitial lymphomatous deposits in the liver, the remaining organs show nothing worthy of note.

CASE XI.—Male, aged fifty-eight, admitted April 8, 1921, died April 9, 1921. The patient stated that in March, 1918, he noticed a swelling in the right side of the neck that gradually increased in size. In February, 1920, a similar swelling appeared on the left side of the neck. In December, 1920, he began to suffer from shortness of breath, followed by difficulty in swallowing and speaking. At the time of admission, about four months later, physical examination revealed a large mass in the left side of the neck, together with enlargement of the inguinal nodes on both sides and of the auxillary nodes on the left side. The left side of the chest bulged markedly and the skin over it was œdematous, the corresponding superficial veins were engorged, and the left arm was œdematous to such an extent as to interfere with motion. There was dullness over the upper half of the left lung anteriorly and posteriorly, and bronchial breathing throughout both lungs. The liver was palpable 3 centimetres below the costal margin. The lower extremities were œdematous.

Autopsy.—Inspection revealed immense swelling and œdema of the left arm and hand. On both sides of the neck were masses of enlarged lymph-nodes that were firmly attached to the skin and to the underlying structures. On the left side of the neck, behind and at about the middle of the sternocleidomastoid muscle, the skin was eroded, giving rise to an irregularly rounded ulcer which measured 5 centimetres in diameter, the edges sloping, the base reddish and granular. In the lower portion of the left axilla was a solitary mass which lay immediately beneath the skin, was somewhat egg-shaped and measured 6 centimetres in length and 3 centimetres in diameter. It was firmly attached to the skin and was only slightly movable against the deeper structures. The inguinal lymph-nodes on both sides were palpably enlarged. On opening the chest, each pleural cavity was found to be occupied by about 250 cubic centimetres of brownish fluid, while a huge tumor came into view in the region normally occupied by the thymus. The tumor measured 17 by 10 centimetres. Its shape was comparable to that of the normal thymus. The growth, extending downward, infiltrated the pericardium and replaced the muscular structures of the right auricle of the heart. It molded itself around the structures at the base of the heart, including the aorta and pulmonary artery, and around the upper part of the œsophagus. Direct extensions from the growth covered the parietal pleura above the apices of the lungs. Near the bifurcation of the trachea, a large nodule projected into the œsophagus, in such manner as to lift the mucosa without, however, producing ulceration. At the bifurcation of the trachea, the larger bronchi were surrounded by tumor tissue. The right bronchus was compressed and its mucosa superficially eroded, while in its walls, particularly posteriorly, were cream-colored islands of tumor tissue. The left bronchus, immediately below the bifurcation, presented five or six cream-colored bands of tumor tissue which ran circumferentially, and replaced the cartilaginous rings for a distance of about 4 centimetres. The mass grew upward into the neck, where the soft tissues were directly and extensively infiltrated, the infiltration extending as far as the level of the lower jaw on both sides and as far backward as the trapezius muscle. Around the abdominal aorta, near its bifurcation, were a dozen or more enlarged lymph-nodes, the largest measuring 4 centimetres in length and 2 centimetres in thickness. In the vicinity of the head of the pancreas were several enlarged nodes, the largest measuring 5 by 3 centimetres. The spleen, which measured 15 by 8 centimetres, was free from indications of tumor growth.

Histology.—Microscopic examination of the growth in the region of the thymus and in the enlarged lymph-nodes in different parts of the body shows a diffuse overproduction of lymphocytes, arranged in an inconspicuous stroma of connective tissue. The histologic changes in the enlarged spleen are those of chronic passive congestion.

CASE XII.—Female, aged thirty-one, admitted November 25, 1925, died December 31, 1925. On admission, the patient complained of dyspnœa which had commenced

suddenly four weeks previously and stated that it was becoming increasingly difficult for her to breathe. She was orthopnœic and examination revealed swelling of the right upper extremity and of the corresponding breast. Expansion was absent over the entire right chest. The heart was displaced to the left, the apex resting in the sixth interspace, 16 centimetres from the mid-line. There was no enlargement of the superficial lymph-nodes. The right chest was tapped and 1,480 cubic centimetres of clear fluid were removed. In the course of the next three weeks, the right pleural cavity was tapped on five occasions, yielding a total of 9,000 cubic centimetres. In spite of the removal of fluid, dyspnœa not only continued but became more distressing, and death supervened.

Autopsy.—On lifting the sternum, an enormous tumor came into view lying in the region of the thymus. The growth, which measured 15 centimetres in length and 8 centimetres in breadth, approximated the shape of the normal thymus. Anteriorly, the tumor was attached to the posterior surface of the sternum, and on the right side, at

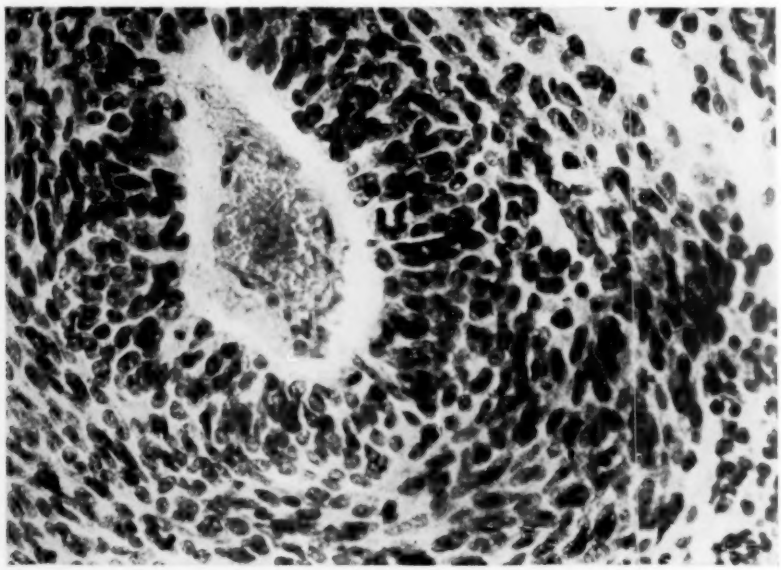

FIG. 6.—High-power photomicrograph from a perithelioma of the thymus, showing a small blood vessel with tumor cells arranged radiately to its long axis and, at the periphery, tumor cells in circumferential distribution.

the third and fourth interspaces, it penetrated and replaced the intercostal muscles over a wide area. Posteriorly the growth extended as far as the root of the lung, molding itself around the aorta, trachea and larger bronchi, and the origin of the carotid arteries. Laterally the tumor infiltrated practically the whole of the parietal pleura on the right side, so that the pleura was thickened to the extent of from 3 millimetres to 1 centimetre, the infiltrating neoplasm presenting a smooth or somewhat undulating surface, with here and there nodular formations, the largest of these being about 1 centimetre in diameter at the base. The tumor at its lower extremity presented a notch which was about 3 centimetres in length, thus dividing the growth into two poles—a right and a left. The right pole extended downward over the pericardium and brought about infiltration of the diaphragmatic pleura, which was thickened from 1 to 4 centimetres. The left pole sent prolongations from its posterior aspect directly through the upper portion of the pericardium, and the intrapericardial portions of the aorta and the origin of the pulmonary artery were infiltrated with nodular tissue, while on the anterior surface of the right auricle, at about its centre, was a solitary nodule fixed to the wall of the

auricle by a base which measured 1 centimetre in diameter, the mass itself being about ½ centimetre in height and mushroom shaped. In the epicardium, corresponding roughly to the course of the left coronary artery, were about a dozen pinhead-sized deposits, and in the wall of the left ventricle laterally, midway between apex and base, were two or three nodules, the largest measuring about 1 centimetre in diameter at the base. In an upward direction, the growth extended to the level of the sternum, but did not infiltrate the structures of the neck. Posteriorly, lying just in front of the spinal column and extending downward as low as the pillars of the diaphragm, were numbers of tumor nodules, directly continuous with the main growth. The right lung was compressed, partly by the tumor itself and partly because of the presence in the pleural cavity of a collection of about 750 cubic centimetres of serous fluid. The left pleura was free. The spleen was normal in size and presented a half-dozen small capsular nodules which, on section, extended into its substance for a few millimetres. The left kidney showed two or three small whitish deposits flush with the surface of the organ and extending downward into its substance for a distance of from 3 to 6 millimetres.

Histology.—Microscopic examination of sections removed from the mass in the thymic region reveals a densely cellular growth of lymphocytes arranged diffusely in an inconspicuous stroma. The same histologic appearance obtains in the enlarged lymph-nodes, and there is identical infiltration of the pleura and the heart muscle.

Case XIII.—A boy, aged seventeen years. On admission, he said that two weeks previously he suddenly became short of breath and was seized by a dull pain in the upper part of the chest, attended by cough and expectoration. On physical examination, both legs were œdematous and the face and neck were cyanotic. On percussion of the chest, there was marked flatness from the clavicles downward. Thoracentesis was followed by the withdrawal of enormous amounts of fluid. The abdomen was similarly distended.

Autopsy.—On opening the thorax, both pleural cavities were found to contain large quantities of fluid, compressing the lungs. Lying in the anterior mediastinum, corresponding to the position of the thymus, was a large, firm mass which extended upward as far as the lower level of the neck and downward in front of the pericardium to the level of the auriculo-ventricular groove. The pericardium was distended by fluid and strewn over both layers was a sheeting of fibrinous exudate. The heart muscle in the upper part of the left ventricle was fleshy in appearance, as if infiltrated by tumor growth. Both kidneys were enormously increased in size, each measuring 15 by 10 by 7 centimetres and weighing, together, 1,040 grams. The retroperitoneal and lower cervical lymph-nodes were moderately enlarged and the bone marrow presented numbers of whitish foci.

Histology.—Microscopic examination of sections from the growth in the region of the thymus shows diffuse proliferation of lymphocytes with scarcely any discernible supporting framework, but with a liberal supply of small vascular channels. Practically identical changes are present in the lymph-nodes. In the visceral pericardium is a thick layer of densely packed lymphocytes. Among the underlying heart muscle fibres scattered foci of lymphocytes are to be seen. The bone marrow exhibits patchy infiltration of the same sort of cells.

Case XIV.—Male, aged fifty-two, admitted December 12, 1929, died April 13, 1930. The patient stated that five months previously he had noticed some difficulty in speech—that he "had to slow down and not get excited or he could not be understood." He gradually found it impossible to make himself understood and had to cease work. Shortly before this he experienced difficulty in swallowing, which became progressively worse. At about the same time he observed that the lower jaw began to droop and that he had to hold it up with his hand, and that the left eyelid sagged. At the time of admission to Bellevue Hospital, the face was expressionless, the neck muscles weak, the patient could not approximate the jaws and it was impossible for him to protrude the tongue. Neurologic examination showed that the right pupil was larger than the left.

The extraocular movements were poor in all directions. There was marked weakness of the fifth and seventh nerves on both sides. The voice was nasal. Otherwise neurologic examination was negative. Death occurred suddenly after an illness of approximately nine months' duration.

Autopsy.—The autopsy findings were without significance in the present connection except for the presence of a growth in the region normally occupied by the thymus. The growth simulated the shape of the thymus and measured 12.5 by 7.5 by 2.5 centimetres. It was cream colored and, on section, its substance was smooth and homogeneous in appearance and fairly firm in consistence.

Histology.—Microscopic examination of the growth shows complete obliteration of the normal architecture of the thymus by the diffuse overgrowth of lymphocytes, which are densely packed in an inconspicuous stroma of connective tissue. Among the lymphocytes are numerous vessels, all of them distended by red cells.

LEUCEMIC CONVERSION OF THYMIC LYMPHOSARCOMATA

Case XV.—Male, aged thirteen years, admitted July, 1923, died September 13, 1923. The patient complained of weakness and pain in the left side of the chest of two weeks' duration. The onset, he said, was sudden and accompanied by cough and a feeling of fatigue. On admission, the skin and visible mucous membranes were pale and the patient was markedly dyspnœic. The left side of the chest bulged noticeably and diminished respiratory movements on that side were accounted for by signs of fluid in the corresponding pleural cavity, the heart being displaced to the right. There was slight general lymphadenopathy. The spleen and liver were not palpable. Thoracentesis was performed four times and a total of over 2,000 cubic centimetres of blood-stained fluid was removed from the left chest. About a month after admission, it was noticed that the spleen was palpable 10 centimetres below the costal margin. The patient became progressively weaker and hæmorrhages occurred into the mucous membrane of the uvula and the inside of the cheek. The liver was now at a level with the umbilicus, and the lower edge of the spleen reached the pelvis. Ecchymosis occurred in the left pectoral region, and purpuric spots appeared round the joints of the elbows, wrists, ankles and knees. On admission, the white blood cells numbered 22,000, of which 50 per cent. were polynuclear neutrophiles, 46 per cent. lymphocytes, and 4 per cent. mononuclears. The blood count on July 26 showed an increase of lymphocytes to 61 per cent., and on September 7 the white cells numbered 97,600 and, of them, 98 per cent. were lymphocytes.

Autopsy.—The body was that of an emaciated, very anæmic boy, in whose conjunctivæ and skin there were numerous petechial hæmorrhages, together with crusted blood about the gums. Both pleural cavities were distended by blood-stained fluid. In the anterior mediastinum, corresponding to the position normally occupied by the thymus, was a massive tumor, which extended downward from the jugular fossa to the level of the crura of the diaphragm and posteriorly to the spinal column, molding the aorta, pulmonary artery and trachea into its substance. On the left side, it brought about extensive infiltration of the diaphragm and of the pleura in the region of the apex of the left lung, the pleura in this situation being thickened and nodular. The liver was enlarged and studded with minute whitish areas. The submaxillary lymph-nodes on the left side were markedly enlarged, as were the axillary and inguinal nodes on both sides, and the mesenteric nodes, all of them discrete and fairly firm to the touch. The spleen was increased in size, weighing 350 grams, but, on section, showed no indications of tumor growth. There were numerous petechial hæmorrhages in the epicardium, in the mediastinal tumor itself, and in many of the lymph-nodes.

Histology.—Microscopic sections from the growth of the thymic region and from lymph-nodes in various parts of the body show thickly cellular lymphocytic collections supported by an almost imperceptible stroma of connective tissue with, in both situations, a sprinkling of small injected blood-vessels. Sections from the pleura reveal infiltration

of its walls by hordes of lymphocytes, the underlying alveoli being compressed. In the diaphragm the muscle fibres are widely separated by myriads of similar cells, in other places the muscle tissues are completely replaced by them. In the liver are large and small interstitial and intralobular collections of lymphocytes, together with the intrusion of many lymphocytes into the blood of the sinusoids.

Case XVI.—Male, aged thirty-eight years, a clerk, admitted December 2, 1924, died December 29, 1924. Little could be learned of his history, except that for two weeks past he had complained of cough and precordial pain. At the time of admission, there was a mass of enlarged lymph-nodes in the left submaxillary region, 5 centimetres in diameter. The left posterior cervical nodes were enlarged, forming a mass 10 by 5 centimetres. Enlarged lymph-nodes were present in both axillæ, those in the right forming a mass about 4 centimetres in diameter. The inguinal lymph-nodes were moderately enlarged. The liver was not felt. The spleen was palpable on deep inspiration under the costal margin in the anterior axillary line.

During the twenty-seven days that the patient was under observation, petechiæ appeared in various parts of the body and, on the ninth day, there was bleeding from the nose. The temperature for the first twelve days pursued an irregular course, averaging 102.5° F. in the evening. For the next six days it varied from 100° to 101° F. and finally became septic in type. The patient now complained of sweats, cough and intermittent dyspnœa. On the second day after admission, the blood count revealed 14,400 leucocytes with a differential count of 9 per cent. polynuclear neutrophiles and 91 per cent. immature lymphocytes. All subsequent counts were virtually the same. The left chest was tapped on three occasions for a total of some 3,500 cubic centimetres of fluid.

Autopsy.—On opening the chest, the anterior mediastinum was found to be completely occupied by a firm wedge-shaped tumor which measured 12.5 by 6 centimetres and which was attached to the lungs on both sides. On the left, an extension ran downward over the anterior surface of the pericardium as far as the diaphragm and infiltrated the pericardium and the anterior margin of the left lung. Lymph-node enlargements were encountered in the neck, axillæ and groins, and there were one or two slightly enlarged nodes in the retroperitoneal region. The rest of the lymphatic system, including the spleen, showed nothing worthy of note.

Histology.—Microscopic sections from the mass in the region of the thymus show a densely cellular growth of lymphocytes in which the cells are arranged in islands of variable shape and size, but in which streak-like formations occur with frequency. In the lymph-nodes the lymphoid cells stain rather less intensely and tend to follow a more diffuse arrangement. In the spleen are numbers of moderately hyperplastic lymphoid follicles, together with a sprinkling of lymphoid cells and fairly numerous lymphocytic clusters lying in the sinuses, the appearance of the spleen as a whole being considerably more cellular than in ordinary circumstances. In the liver are to be seen minute aggregations of lymphocytes, particularly in the interstitial connective tissues, and many lymphocytes in the blood of the sinusoids.

Case XVII.—Male, aged four years, admitted March 7, 1927, died April 19, 1927. Eight weeks before admission, he developed signs of fluid in the left chest. The chest was tapped on six occasions and each time bloody fluid was obtained. On admission to the hospital, the child was pale, weak and dyspnœic. All of the superficial lymph-nodes were enlarged to a moderate extent. During the six weeks that the child was under observation, the left arm became so œdematous that he could not move it and the left chest was tapped on three occasions, a total of 690 cubic centimetres of clear brownish fluid being withdrawn. The heart was markedly displaced to the right. During the interval of observation, œdema spread to include the face and neck, the right arm, and the right foot and leg. Ten days before death, petechiæ and purpuric spots appeared in the skin. Numerous blood-counts revealed a leucocytosis varying from 15,700 to 50,000,

and the lymphocytes numbered between 66 and 95 per cent. Death occurred sixteen weeks after the onset of symptoms.

Autopsy.—The lymph-nodes of the cervical, axillary and inguinal regions were palpable and varied in size from a small lima bean to an almond. The anterior mediastinum was filled by a large tumor adherent to, but not infiltrating, the sternum. The mass extended from the suprasternal notch to the diaphragm. It measured 16 centimetres in length, 10 centimetres in breadth and 8 centimetres in depth and simulated the shape of the thymus. The great vessels at the base of the heart were surrounded by the growth, which crossed the hilum of the lungs and descended behind the heart for a short distance. The mass was adherent to the parietal pericardium, but did not perforate it at any point, although the pericardium was completely surrounded by new growth except for one or two small oval areas. Anteriorly the tumor decussated at the pericardial attachment to the diaphragm and spread in a thin layer over the median portions of the diaphragmatic pleuræ and along the pleura covering the adjacent portions of the vertebral column. The lymph-nodes at the root of the lung were greatly enlarged. In the lower portion of the abdomen, the mesenteric and retroperitoneal lymph-nodes were slightly enlarged, the largest nodes being about ½ centimetre in length. The lymph-nodes in the region of the head of the pancreas were similarly involved as were those in the gastrohepatic omentum and around the junction of the common and cystic ducts. The spleen weighed 90 grams and, on section, the follicles were prominent. The spleen was natural in shape.

Histology.—Microscopic examination of the tumor in the thymus shows the presence of diffuse overgrowth of cells which are noticeably larger than the small lymphocytes and whose nuclei stain much less intensely. The cells are so closely packed that even under the oil immersion lens their individual shapes cannot be determined. In the secondary deposits, however, notably in the lymph-nodes, where the cells are more loosely arranged, examination under the oil immersion lens shows a small amount of cytoplasm and a relatively large nucleus, with few chromatic particles in it. The nucleus in some instances is rounded, in others it shows a slight indentation, and in still others it has a reniform appearance caused by a deep indentation at about its centre on one side. As far as can be told from fixed tissues, this cell corresponds to the large mononuclear lymphocyte or the transitional cell of Ehrlich's classification or to the monocyte of the modern hematologist. According to this interpretation, the patient died of acute monocytic leucemia.

HODGKIN'S DISEASE

CASE XVIII.—Male, aged forty-six, admitted February 22, 1930, died four days later. The patient complained of shortness of breath of twelve weeks' duration. Physical examination on admission showed, in addition to dyspnœa, swelling of the ankles that, according to the patient, had been present for a period of four weeks, while the hands in the course of the past week had likewise commenced to swell. The face was cyanotic. The superficial veins of the neck were prominent and there was dullness over both upper lobes, especially on the left side, where the breath sounds were hoarse. Abdominal breathing was marked, and the superficial veins in the abdominal wall were prominent. X-ray examination revealed a massive growth in the upper anterior mediastinum, completely replacing the upper lobe of the right lung.

Autopsy.—On removal of the sternum, a massive growth came into view. It measured 14 centimetres in length and 15 centimetres in breadth and extended deeply into the thorax. It was grayish white in color, firm, with a slightly undulating surface and completely filled the superior anterior mediastinum, displacing the heart and pericardium downward, the mass forming a sort of bridge between the lungs. The growth extended laterally, invading the anterior borders and replacing the substance of the upper lobes of both lungs for a distance of from 4 to 5 centimetres. It extended into the neck, particularly on the right side, in the form of two or three cords, dividing the lobes

of the thyroid. In the superior mediastinum the tumor embraced all the great vessels at the base of the heart, including the arch of the aorta and its branches, the pulmonary artery, the superior vena cava, and the subclavian veins, compressing but not invading or occluding them. The superior vena cava was invaded, and two or three cord-like extensions of tumor tissue projected into the lumen of the vein, growing directly downward, where they entered into the cavity of the right auricle. Inferiorly, the growth which pushed the pericardial sac downward, also invaded that cavity in its upper part, without, however, infiltrating the origin of the great vessels within the pericardium or the heart muscle. Posteriorly it eroded directly into the trachea and right bronchus, the eroded portions appearing as cream-colored areas several centimetres in length on the right side of the trachea, and extending thence for several centimetres into the walls of the corresponding bronchus.

Histology.—Microscopic examination shows the presence of a diffuse overgrowth of lymphocytes lying in a fibroblastic stroma. Among the lymphocytes is an occasional cell of the large mononuclear variety and, rarely, a multinucleated cell of the myeloid type.

CASE XIX.—A woman, fifty-six years of age, who complained of palpitation of the heart, shortness of breath and a cough of four months' duration, followed in the next three months by dilatation of the veins of the upper side of the chest on the left side, œdema of the corresponding portion of the chest wall and of the arm and, finally, by generalized œdema; dyspnœa followed by orthopnœa, and death six months later or thirteen months after the onset of symptoms.

Autopsy.—There was a mass in the upper and anterior mediastinal regions, corresponding in its outline to that of the thymus. The mass measured 18 centimetres in a downward direction and 11 centimetres transversely. It projected through the upper aperture of the thorax and invaded the right lobe of the thyroid for a distance of 3 centimetres. The mass compressed the upper lobe of the right lung and extended backward around the great vessels at the base of the heart, where it compressed the trachea and displaced it to the right, penetrating its walls for a distance of 8 centimetres without producing ulceration of its mucous membrane. The left pleural sac contained 1,350 cubic centimetres of fluid. The spleen was not involved.

Histology.—Microscopic examination of the mediastinal growth and of its extensions into the thyroid and trachea shows the presence of preponderating numbers of lymphoid cells, among which are mononuclear and multinuclear giant cells, the latter of the lobulated or myeloid type, a few plasma cells, and numbers of eosinophiles.

CASE XX.—Male, aged twenty-seven, admitted May 30, 1930, died October 18, 1930. Six years before admission the patient developed an enlarged node beneath the right ear. The node was removed and microscopic examination showed the histology of Hodgkin's disease. The patient stated that in the course of six years he had developed at various times similar enlargements in the left side of the neck and in the axilla, for which, at intervals, he had received X-ray exposures, the nodes apparently remaining stationary during treatment and enlarging when treatment was discontinued. A year before entering the hospital the patient gave up work because of increasing weakness. On admission to the hospital, the spleen was palpable just below the costal margin, and marked enlargement of the lymph-nodes was noted beneath the angle of the left jaw and in the region of the mastoid process on the right side, in the right axilla, in both supraclavicular fossæ, and in both groins. The patient complained of no pressure symptoms until six weeks after admission, when he stated that there was a distressing sensation of pressure "deep" in the chest behind the middle of the sternum. About two months after this, he began to complain of difficulty in swallowing. Death occurred three months and one week after the onset of pressure signs within the thorax.

Autopsy.—On inspection, the body showed marked enlargement of the nodes in the neck below both ears and in the axillary region. In the region of the thymus there was a growth which measured 12 by 6 by 4 centimetres. It lay directly in the mid-line

between the lungs, extending from the level of the suprasternal notch above to the auriculo-ventricular groove below, and presented an indentation at its lower pole. On the left side it was entirely free; on the right side it infiltrated the anterior border of the lung for a distance of 4 centimetres in a lateral and 6 centimetres in a downward direction. The growth surrounded and compressed all the great vessels at the base of the heart and wrapped itself around the trachea in such form as to present isolated nodules posteriorly between the trachea in front and the œsophagus behind. It penetrated the upper and anterior portion of the pericardium in the form of twenty or more, large or small, rounded, oval or undulating, fused masses, presenting, on section, exactly the same naked-eye appearance as that of the original growth in the thymic region. One of these masses, which measured 4 centimetres in breadth, 2 centimetres in thickness and 2 centimetres in depth, lay directly in the anterior wall of the aorta. Similar but smaller nodules were to be seen in the wall of the pulmonary artery at its commencement. The pericardium enclosed 350 cubic centimetres of dark amber-colored fluid containing quantities of soft, somewhat gelatinous material. Both layers of the pericardium were diffusely covered with fibrinous exudate. The peribronchial lymph-nodes were enlarged, measuring from 1 to 5 centimetres, some of them discrete, others fused; all of them were infiltrated. Section of the right lung through the area of infiltration showed the presence of huge quantities of new growth extending into the substance of the lung for a distance of about 5 centimetres, the invading tissue being arranged for the greater part around the smaller bronchi, frequently occluding or partially occluding their lumina. Between the individual small bronchi, the lung tissue was diffusely infiltrated by new growth. The spleen was enlarged; it weighed 425 grams and measured 16 by 11.5 by 4 centimetres. Projecting beneath the capsule were numerous white masses of irregular size which, on section, were so richly distributed through the splenic pulp as almost completely to replace it. At one end, in fact, about half of the spleen was almost completely replaced by a firm, pearly gray growth which projected above the surface in the form of closely packed, pinhead-sized or larger foci. The liver weighed 2,800 grams and appeared to be well preserved. The retroperitoneal lymph-nodes were closely packed and lay on either side of the vertebral column, forming a mass about 20 centimetres long, 10 centimetres in thickness and 10 centimetres in width.

Histology.—Microscopic examination of tissues removed from various parts of the body shows the histologic changes characteristic of Hodgkin's disease. In the lymph-nodes the architecture is completely replaced by the overgrowth of connective tissue which, for the greater part, is thickened and hyaline and encloses variable numbers of lymphocytes and innumerable mononuclear and multinuclear giant cells.

Case XXI.—Female, aged thirty-two, admitted May 1, 1917, died June 17, 1917. She complained of "asthmatic" attacks of two years' duration. In the past year difficulty in breathing had increased to such an extent that she was unable to lie down night or day. At the time of admission orthopnœa was distressing and both upper extremities and the anterior chest wall were œdematous. Over the right side of the chest anteriorly the percussion note was flat and expiration was high-pitched and hissing, although not frankly bronchial, and the voice sounds were high-pitched and increased in quality. The spleen was not felt. The edge of the liver was palpable about 5 centimetres below the right costal slope, and there were signs of fluid in the left chest. During the seven weeks that the patient remained in the hospital, the left chest was tapped five times and on each occasion from 1,000 to 1,500 cubic centimetres of fluid were removed. The X-ray report was to the effect that there was a large area of diminished illumination in the right pulmonic field, which was interpreted as due to a tumor in the anterior mediastinum.

Autopsy.—The anterior chest wall was œdematous. On opening the body a growth was apparent in the region normally occupied by the thymus. The growth measured 25 centimetres in length and 18 centimetres in thickness and was firm in consistence. It presented a whitish or faintly cream-colored substance and extended downward in

such manner as to obliterate the upper part of the right pleural cavity and to invade and replace almost the whole of the two upper lobes of the right lung. The lower lobe of the lung was not involved. Scattered through the substance of both lungs were numbers of large and small, circumscribed nodules made up of tissue of identical appearance with that in the main growth. The peribronchial nodes were greatly enlarged, as were those lying at the sides of the œsophagus. The cervical and abdominal nodes were unchanged. The left pleura enclosed about 2,000 cubic centimetres of clear yellow fluid. The spleen was slightly enlarged, but was not nodular.

Histology.—Microscopic examination of the growth in the thymic region shows a connective tissue reticulum supporting great numbers of lymphoid cells, among which are prominent numbers of large mononuclear cells and an occasional multinuclear giant cell of the myeloid type. Microscopic examination of the peribronchial lymph-nodes reveals large collections of lymphocytes, among which are mononuclear and multinuclear giant cells, the islands being separated by rather coarse bands of mature connective tissue. In places these islands are permeated and partially or completely replaced by a dense, pinkish staining, poorly nucleated, hyaline reticulum, such as has been described as a local attempt at healing. The nodules in the lung are made up almost exclusively of lymphoid cells, but among them are disclosed a few mononuclear giant cells and, rarely, a multinuclear cell of the myeloid type. Moderate numbers of eosinophiles are to be seen, usually at the periphery of the lymphoid collections. The spleen, and liver microscopically are well preserved.

Case XXII.—Male, aged forty-four, admitted April 30, 1931, died June 13, 1931. On admission, the patient stated that in 1928 he noticed that he became short of breath on exertion, that this was slowly progressive and that he was easily fatigued. About six months later he experienced a choking sensation on exertion. Shortly after that he detected a swelling in the neck and observed that there was loss of some twenty pounds in weight. Shortly after admission he developed a dry cough and complained of itching of the skin. Deep X-ray therapy relieved considerably the dyspnœa and cough and the patient was discharged from the hospital improved. About five months later he was readmitted complaining of return of his original symptoms. At this time, physical examination revealed marked orthopnœa, cyanosis, œdema of the left upper extremity and of the corresponding side of the chest and leg, together with signs of an effusion into the pericardial sac.

Autopsy.—On opening the chest, an enormous mass came into view lying in the middle line and occupying the space normally assigned to the thymus. The mass measured 18 centimetres in length, 7.5 centimetres in width at the upper level of the manubrium, and 6 centimetres at the inferior margin. The growth resembled the shape of the thymus, decussating at its lower end to form a distinct notch. The mass was solid in consistence, whitish in color. It insinuated itself around the structures at the base of the heart and was firmly attached to the pericardium. It was fixed to the anterior margin of the right lung and on the left side penetrated deeply into the substance of the lung, almost completely replacing the upper lobe. Below, the growth sent a prolongation downward over the pericardium into the diaphragm. Above, the growth was continuous with an irregularly nodular mass lying in the lower part of the right side of the neck. The growth extended into the upper portion of the pericardium and set up within the pericardium a collection of yellowish nodular masses, almost completely obliterating the upper third of the cavity. The muscle substance of both auricles and of the upper third of the right ventricle, both anteriorly and posteriorly, was apparently completely replaced by nodular deposits. The retroperitoneal lymph-nodes in the region of the pancreas were greatly enlarged. There were a few enlarged, discrete lymph-nodes in the region of the internal abdominal ring on both sides. The spleen was normal in size and, except for congestion, showed no naked-eye changes. The same was true of the liver.

Histology.—Microscopic examination of sections removed from lymph-nodes in various parts of the body reveals complete obliteration of the normal architecture and replacement by connective tissue overgrowth, the fibrils of which in many places are markedly sclerotic. Scattered through the connective tissue interstices are moderate numbers of round cells of the lymphocytic type and relatively very large numbers of mononuclear and multinuclear giant cells, together with a few eosinophiles. Microscopic examination of the liver and spleen shows no histologic indications of Hodgkin's disease whatsoever.

THE EPITHELIOMATA

CASE XXIII.—Male, aged fifty-six, admitted to Bellevue Hospital July 7, 1930, died August 13, 1930. The patient stated that one morning four weeks previously he awakened with a stiff neck. Since that time his head tended to fall forward and in the past two weeks he has had to support his head with his hands. At the same time the patient complained of some difficulty in swallowing, regurgitating fluid through the nose. He also complained of progressive difficulty in chewing and on several occasions had to be fed by a stomach tube. Neurologic examination revealed a left-sided Horner's syndrome, weakness of the left side of the palate and deviation of the tongue to the left. All the neck muscles were weak. The muscular power of the limbs was entirely normal. The neurologic findings were otherwise negative. The patient remained in the hospital for a period of about five weeks and died suddenly in an acute attack of dyspnœa attended by cyanosis. During his stay in the hospital the patient was regarded as suffering from a high cervical and bulbar lesion, probably of vascular origin.

Autopsy.—On removing the sternum, the superior mediastinum corresponding to the position normally occupied by the thymus showed a growth which was roughly "heart shaped," with the notch downward. The tumor measured 7 centimetres in length, 5 centimetres in width, and 3 centimetres in thickness. The right border was free; the left border was attached to the anterior margin of the upper lobe of the left lung, into the substance of which it penetrated for a distance of several centimetres. Below, the tumor rested on the anterior surface of the pericardial sac to which it was adherent, but through which it did not penetrate. The consistence of the tumor was firm and, on section, its substance was white and granular. There were no secondary deposits in any part of the body.

Histology.—Microscopic examination of sections removed from various parts of the tumor shows complete disappearance of the normal arrangement of cortex and medulla. On the other hand, the tumor, particularly in its more centrally situated parts, is made up of large numbers of epithelial reticulum cells and relatively small numbers of lymphocytes. The epithelial reticulum cells are large, irregular in shape, distinct in outline, and are characterized by the presence of a scanty, pale-staining cytoplasm, enclosing a large vesicular nucleus provided with an eccentrically placed acidophilic nucleolus and by the presence of delicate cytoplasmic fibrils. In places these epithelial reticulum cells occur singly, in other areas they are arranged in small groups, sometimes as large islands. Perhaps the most striking feature in the whole microscopic picture is to be found in the concentric condensation of the epithelial reticulum cells to form Hassall's corpuscles. These latter bodies are present in all stages of development, from the early grouping of reticulum cells, through the stage of concentric lamellation, to the final stage where the cytoplasm of the centrally situated cells has undergone granular or hyaline degeneration, the nuclei shrunken and pycnotic. Where the tumor invades the lung tissue there are numbers of epithelial reticulum cells which are arranged in insular formation, with a scant admixture of lymphocytes and no tendency in the direction of whorl formation.

CASE XXIV.—A man, fifty-eight years of age, who, on admission to the hospital, complained of severe burning pains in the back that had been present for three weeks.

Three days before admission, these pains became so excruciating that he was unable to stand and had to give up his work and take to his bed. In addition, he complained of pain in the upper sternal region on swallowing. At the time of admission the entire dorsal spine was rigid and rigidity was increased by movements of the trunk. Two weeks later, the patient could not move the body below the waist. The superficial reflexes were abolished. The knee jerks were preserved and the patient was insensible to pain up to a girdle point about 5 centimetres above the lower border of the ribs. On the following day there were complete paralysis and anæsthesia of the entire body below the level corresponding to the fifth dorsal segment. The knee jerks had now disappeared and there was a bilateral Babinski. The patient suffered from retention of urine and was incontinent of fæces. The spinal column was opened, surgically, from the fourth cervical to the second dorsal vertebræ and a tumor was removed that measured 6 by 2.5 centimetres. In the succeeding three months the patient gradually failed and death occurred.

Autopsy.—On opening the thorax, a mass came into view corresponding to the position normally occupied by the thymus. The mass measured 10 by 8 by 3 centimetres and was roughly triangular in outline with the base upward. It was attached to the margin of the left lung for a distance of about 6 centimetres but was otherwise free. Both lungs were studded with metastatic nodules, varying in size from 1 to 2 centimetres. The spinal cord corresponding to the excised laminæ was markedly compressed and there was a wart-like metastatic growth in the dura at about the level of the third dorsal vertebra.

Histology.—Microscopically, the fibrous ground substance divides and subdivides in such manner as to segregate the tumor cells into groups which vary markedly both in size and shape. Perhaps the commonest variety is a rather small cell with a deeply chromatic homogeneous nucleus. Under ordinary magnification, this cell appears to be rounded and of about the size of a lymphocyte, but, when viewed under the oil immersion lens with properly diminished illumination, it is seen to be irregularly rounded or even polyhedral and to possess a quantity of pale, smooth, or finely granular cytoplasm. This appears to be the cell of origin of the tumor and it may be traced through various transitional stages until it acquires a flattened form. These flattened forms give rise to still larger cells of variable morphology. A noticeable feature is that they show attempts to become arranged in whorls and thus to present a resemblance to Hassall's bodies.

SPINDLE-CELL SARCOMA

Case XXV.—Male, aged forty, admitted December 2, 1930, died December 8, 1930. In June, 1930, the patient's illness commenced with cough and expectoration and anorexia. He remained at work until September 1, when he had to discontinue because of weakness. In that length of time his chest was tapped on five different occasions. The patient stated that he was short of breath before the tapping and somewhat relieved by it. Two months before admission he became markedly dyspnœic, dyspnœa finally changing to orthopnœa. At the time of admission, he was orthopnœic and slightly cyanotic. The right chest showed signs of fluid. At this time the patient stated that he had recently noticed that it was becoming increasingly difficult for him to swallow, either solid or liquid food.

Autopsy.—In the anterior and superior mediastinum, extending from the level of the suprasternal notch downward in the middle line in front of the pericardium as far as the apex of the heart, was a tumor which was irregularly nodular but which simulated the shape and occupied the position of the thymus. It measured 17 centimetres in a downward direction, but was otherwise too indefinite in distribution to be measured even with approximate accuracy. At the base of the heart it molded itself around all the great structures, including the aorta, the carotid vessels, trachea and œsophagus, burying them in a solid mass of tumor tissue. Posteriorly it extended into the right

lung along the connective tissue planes surrounding the bronchi, along which it traveled fan-fashion to the extreme base of the right lower lobe, compressing but not invading the large bronchus just after its bifurcation, except for the presence of some ten or fifteen whitish, submucous elevations which had not gone on to the process of ulceration. The left lung was free. Posteriorly the tumor extended from the level of the suprasternal notch downward to the body of the seventh thoracic vertebra; in other words, for a distance of approximately 15 centimetres. Anteriorly the tumor extended directly into the upper aspect of the pericardial sac and into the posterior part of the auricle, where it presented itself as a large, irregularly-outlined, cream-colored, mound-like projection which measured 7 centimetres in length and 4 centimetres in breadth. The endocardium covering this projection was intact. Posteriorly the tumor likewise projected itself into the pericardium at its upper aspect and into the posterior wall of the left auricle, where it presented itself as an irregularly outlined, mound-like growth, representing a replica of the one in the opposite auricle, except for the fact that the one in the left auricle was larger. Posteriorly the tumor at one point directly invaded the œsophagus in the form of a soft, cream-colored, mushroom-like growth, measuring about 1 centimetre in diameter and 3 millimetres in height; this lay at the level of about the fifth thoracic vertebra.

Histology.—Microscopic examination shows a dense fibroblastic stroma imbedded in which are large and small islands of small, rather richly chromatic tumor cells. Many are spindle, others oat shaped. These two differently shaped cells are present in about equal proportions, one or the other type preponderating, however, in different parts of the tumor. Except for the absence of any vascular unit, the shape and arrangement of the cells reminds one very much of perithelioma. In the absence of any vascular unit, however, this diagnosis seems scarcely justified and the tumor appears to be best classified as a spindle-cell sarcoma arising from the connective tissue framework of the thymus.

GROWTH BEHAVIOR

Many of the thymic growths here recorded presented features of growth behavior which made it possible, within certain limits, to trace their evolution with something approaching a consecutive course. In three of the cases, the growths were obviously in an early stage of development. In one of them, the tumor—a reticulum-cell epithelioma with reproduction of Hassall's bodies—was encountered at autopsy as an accidental finding. It presented itself as a solid mass which occupied the position of the thymus and was "heart shaped." The base was unattached and directed upward, the notched apex downward. The growth was attached to but did not penetrate the pericardium. Its right border was free. The left border was fixed to the margin of the lung and penetrated along the line of the bronchus for a distance of 2 or 3 centimetres. In a second case the growth in the thymus—a perithelioma—was unattached except for the fact that it grew downward and penetrated the right lung along the line of the large bronchus. As illustrating the perversity of neoplasmic behavior, in a third case—an epithelioma of the thymic remains—the original growth was comparatively small in size and was attached only to the margin of the left lung. In addition, however, the lungs were riddled with metastatic deposits and a large metastasis in the upper spine so effectually compressed the cord as to bring about complete paraplegia. Thus, it appears that thymic growths, early in their evolution, display a tendency mechanically to infiltrate the lungs. Their subsequent

behavior is such as to bring about an array of destructive changes in the thoracic viscera that is seldom paralleled in the domain of disease—penetration of the pericardium and invasion of the heart muscle; infiltration of the pleura, sometimes as isolated nodules, oftener over a diffuse or prairie-like expanse; compression and invasion of lung tissue involving one, sometimes two or more lobes, often with secondary infection and abscess formation; infiltration of adjacent muscles, such as the intercostals and the diaphragm; compression and infiltration of the œsophagus, trachea and bronchi, and of the walls of such great vessels as the aorta, pulmonary artery, the innominate and jugular veins and the superior vena cava; enlargement of lymph-nodes, metastatic or otherwise, in different parts of the thorax, sometimes elsewhere; and, finally, by such effects as are revealed by the transudation of enormous quantities of fluid into the pleural and pericardial sacs, the peritoneum or subcutaneous tissues. Although in most of these cases by far the greater burden of attack is borne by intrathoracic structures, the program of destruction not uncommonly is extended to include metastatic deposits in extrathoracic viscera, among them secondary lesions in the lymph-nodes in various parts of the body and in the liver, adrenals, pancreas, thyroid, kidney and bones, the peritheliomata, in this respect, displaying particularly vicious qualities.

Infiltration of the Pericardium and Heart.—Of the twenty-five cases of tumors and tumor-like growths of the thymic remains, the pericardium was invaded sixteen times (64 per cent.)—six times by lymphosarcoma, six times by perithelioma, once by a spindle-cell sarcoma, and three times in Hodgkin's disease. Of the six lymphosarcomata, the heart muscle was invaded five times. Of the six cases of perithelioma, the heart muscle was invaded once. In one of the three cases of Hodgkin's disease, the heart muscle was extensively replaced.

Even from this small series of cases, it is evident that tumors of the thymic remains, notably the lymphosarcomata, show a marked inclination to infiltrate the pericardium and to invade the heart muscle. Penetration of the pericardium occurs practically always at the upper end of the sac, obviously because the pericardium lies directly in the pathway along which the growth finds it easiest to travel. In about one-half of the Bellevue Hospital series, the upper end of the pericardial sac presented multiple nodules which projected themselves into the cavity and stopped there. In other instances the tumor nodules advanced to include the walls of the intrapericardial portion of the aorta and the origin of the pulmonary artery, with or without associated changes in the heart muscle itself. Infiltration of the pericardium alone is a comparatively harmless procedure, since it usually occurs in nodules of such size, numbers and distribution as apparently to offer slight, if any, embarrassment to the movements of the heart, although it sometimes happens that they are apparently directly concerned in the initiation of exudates into the sac.

On the contrary, invasion of the heart muscle, in many instances at least,

is so extensive as obviously to impede the action of the heart and thus to contribute its share to those processes which conspire to terminate life. Here, again, the lymphosarcomata are the growths most frequently concerned. In one case of thymic lymphosarcoma the pericardium contained 200 cubic centimetres of fibrino-purulent exudate, the epicardial fat was diffusely infiltrated by tumor growth, the walls of both ventricles were thickened and rigid and were replaced to an almost unbelievable extent by tumor infiltrate, only islands of reddish musculature showing through at intervals. Microscopic examination of the heart wall showed the incursion of lymphocytes to the amazing extent that almost every individual fibre was separated from its fellow by a dense infiltrate of tumor cells, while the fibres themselves were compressed and their striations lost. In a second case both auricles were replaced and the epicardial fat of the right ventricle was infiltrated. In a third case the intrapericardial portion of the aorta and the commencement of the pulmonary artery were invaded by nodules of tumor tissue, in the anterior wall of the right auricle was a solitary nodule 1 centimetre in diameter at its base, the epicardial fat of the left ventricle was sprinkled with small nodules, and in the wall of the left ventricle were two or three nodules, the largest measuring about 1 centimetre in diameter at its base. In a fourth case the pericardium was distended by fibrino-purulent exudate and the heart muscle in the upper part of the left ventricle was replaced by tumor tissue. In a fifth case the muscular structures of the right auricle appeared to be completely replaced by tumor growth. In a sixth case both auricular walls posteriorly were extensively invaded by a perithelial sarcoma. In a case of Hodgkin's disease, on the other hand, the muscle tissues of both auricles and of the upper third of the right ventricle, anteriorly and posteriorly, were practically completely replaced by new growth, the degree of invasion representing the most extensive thus far encountered in our experience at Bellevue Hospital.

The Pleura, Bronchi and Lungs.—Growths of thymic origin show a propensity for invasion of the pleura, sometimes diffusely over a limited area, sometimes by metastatic nodules, but oftener covering vast sweeps of territory. In nine of the twenty-five cases in this series, the pleura was diffusely infiltrated in seven—five times by lymphosarcoma and twice by perithelioma. In the remaining two cases, both of them peritheliomata, the pleura was studded by metastatic nodules. As exemplifying the extent to which diffuse invasion of the pleura may occur, in one case of thymic lymphosarcoma the entire parietal and diaphragmatic pleura on the right side measured 0.5 centimetre in thickness. In a second case the whole of the parietal pleura on the right side was greatly thickened and presented a smooth, sheet-like, or, in places, an undulating surface. In one case a perithelioma of the thymic remains infiltrated both the parietal and visceral pleuræ on the left side, and in a second case the pleura covering the whole of the base of the right lung was similarly infiltrated.

In ten of the twenty-five cases of thymic tumors, the larger bronchi were

buried in tumor tissue. In ten cases the walls of the bronchi were infiltrated for variable distances and their lumina were encroached upon, sometimes almost completely occluded. This occurred four times in lymphosarcoma, four times in perithelioma, and twice in Hodgkin's disease.

In fourteen of the twenty-five cases the lungs were involved, oftenest the upper lobes, three times by compression and eleven times by infiltration. Occasionally the tumor would attach itself to the margin of one or both upper lobes, with a slight but nevertheless appreciable degree of infiltration of the lung substance. In two cases, however, both of them peritheliomata, the upper lobe of the right lung was practically completely replaced by tumor tissue and in one case almost two entire lobes of the right lung were invaded in Hodgkin's disease. In another case of Hodgkin's disease practically the whole of the upper lobe of the left lung was replaced.

Symptoms and Signs, Diagnosis and Prognosis.—In tumors and tumor-like growths of the thymus and its remains, the absence of early signs, if I may so express myself, is one of the most frequent and dangerous symptoms. It is an example of the marvelous adaptability of tissues to the gradual incursions of a new growth and illustrates the extent to which disease may proceed without displaying any sign by which its presence may be detected. Growths of the type under discussion may so expand locally and infiltrate regionally as to bring about destructive changes in the thoracic viscera of such proportions as to excite wonder that the body could withstand these handicaps for so long a period, and yet the patient may carry this burden of disease for many months with no obvious signs of suffering. It is possible that the growth may be suspected if, in the examination of the chest, the heart dullness continues upward toward the suprasternal notch, merging into flatness, and if, in the absence of aortic disease, there is dullness on either side of the manubrium in the first and second interspaces. If such signs are detected, particularly in association with early pressure changes, such as intermittent dyspnœa or hoarseness, or with unexplained superficial enlargements, lymph-node or otherwise, or with the signs of myasthenia gravis, attention should be focussed on the possibility of a thymic growth and confirmation sought by fluoroscopic or X-ray examinations, especially from the lateral aspect, and by microscopic investigation of any nodules which may be removable. Later, when the anatomical factors of safety are neutralized or exhausted, the effects of increased intrathoracic pressure are apt to assert themselves abruptly and to advance relentlessly—orthopnœa, cyanosis, cough, difficulty in swallowing, speech disturbances, inequality of the radial pulses, engorgement of the superficial veins, œdema of the chest wall and arms and sometimes of the legs, effusions into one or more of the thoracic serous sacs or into the peritoneum, and death within a few weeks or months after the initial manifestation of intrathoracic pressure disturbances.

In any event, accurate diagnosis of the variety of growth present is imperative from the standpoint of treatment and prognosis, and is to be predicated largely on the removal and microscopic examination of any

nodules which may be accessible. If it be shown that the lesion is that of lymphosarcoma or Hodgkin's disease, appropriate X-ray treatment, as already mentioned, may provide at least temporary relief from the horrors attendant on increased intrathoracic pressure. In epithelioma and the perithelial and spindle-cell sarcomata, improvement, on the contrary, temporary or otherwise, is scarcely to be anticipated.

The Leucemic Conversion of Lymphosarcoma of the Thymus.—The term leucosarcoma was introduced by Sternberg[7] to denote a condition characterized by the presence in some part of the body of a tumor composed of lymphoid cells which are eventually poured into the blood in such numbers as to constitute a true leucemia. Two types of leucosarcoma are recognized: One, in which the original growth is made up of cells of the lymphoid variety, subsequent invasion of the blood stream representing a form of lymphoid leucemia; a second, in which the original focus of growth is composed of myelocytes, the discharge of which into the blood gives rise to leucemia of the myeloid type. Sternberg records eight cases, six of which were lymphoid and two myeloid. In four cases of the lymphoid variety the original growth was located in the upper anterior mediastinum corresponding to the position normally occupied by the thymus or its remains. In the three cases of lymphoid leucosarcomatosis here recorded, the primary foci of growth were likewise to be found in lymphosarcomata of the thymus.

The recognition of lymphoid leucosarcoma depends, first, on the existence of a tumor in some part of the body that, on microscopic examination, reveals the histological picture of lymphosarcoma, the cells of which, contrary to the usual arrangement, consist almost exclusively of large lymphocytes with an admixture of small cells. In occasional instances this order is reversed. In the greater number of examples of leucosarcoma thus far recorded, however, the large lymphocyte was described as the preponderating cell, both in the primary focus of growth and in the blood. In other instances, on the contrary, the cells in both places have been described as of the type of small lymphocytes. Second, the original focus of growth may exist for weeks, months or years before invasion of the blood stream occurs, but involvement of the blood, when it does take place, is abrupt, and the process then advances with astonishing rapidity.

Thymic Growths and Myasthenia Gravis.—The condition known as myasthenia gravis is characterized by unusually rapid fatigability of certain muscles, notably those of the jaw, larynx, the muscles of deglutition, the upper eyelids and of the face, sometimes of the muscular system as a whole. The condition is so often associated with neoplasmic lesions of the thymus as strongly to indicate an etiological relationship between them. In the majority of cases thus far recorded, the original thymic growths were lymphosarcomata. Mandelbaum and Celler's case, on the other hand, was a perithelioma, and, of the two examples recorded in this paper, one was a reticulum-cell epithelioma, the other a lymphosarcoma. In certain of the recorded cases, minute collections of lymphocytes have been described, not alone in the

muscle tissues in various parts of the body, but in the liver, adrenal, thyroid, kidney, peripancreatic fat and elsewhere. They were found in the muscle tissues in the second case described in this paper, namely, a thymic lymphosarcoma. In such circumstances, however, it is difficult to conceive of any reciprocal relationship between myasthenia gravis and lymphocytic collections in the localities named, and, indeed, it is yet to be determined if such cell foci deviate materially from apparently identical collections in the tissues in conditions which do not depart noticeably from the normal. Nor does it seem reasonable to incriminate any particular type of thymic growth as an instrument in the causation of myasthenia gravis—it is apparently some disturbance of function produced by the growth, rather than the nature of the growth itself that is to be invoked as an explanatory factor. Nevertheless, myasthenia gravis and thymic neoplasms occur sufficiently often in company with one another to warrant investigation of the thymic region in every case in which the symptoms of myasthenia gravis present themselves. In view of the fact that lymphosarcoma assumes such a prominent rôle among neoplasms of the thymus and since this type of growth is not uncommonly amenable to treatment, the clinical detection of its alliance with myasthenia gravis assumes a place of great importance.

SUMMARY

1. At least five different types of malignant tumors or tumor-like growths are capable of arising in the thymus or its remains, namely, perithelioma from the connective tissue of the walls of small blood vessels; lymphosarcoma from the lymphocytic elements; epithelioma from the epithelial reticulum cells; spindle-cell sarcoma from the connective tissue framework and, finally, Hodgkin's disease, which finds in the lymphocytes of the thymus those cells that appear to be prerequisite for its development.

2. Of these five varieties of new growth, the lymphosarcomata and Hodgkin's disease are favorable types for treatment by radiation, in which circumstances the outlook is not altogether without promise. On the other hand, the peritheliomata, epitheliomata and spindle-cell sarcomata, as treatment is now practiced, are hopeless from the outset. Perhaps in the latter connection it is not trespassing too far to prophesy that at least some of these growths may eventually be approached surgically. In such an event, early diagnosis is, of course, imperative. For example, in Case XXIII recorded in this paper, a small epithelioma of the thymus was associated with the signs of myasthenia gravis and, except for the fact that it infiltrated the margin of the left lung, the growth lay otherwise free within the thorax and offered, apparently, the possibility of surgical removal of an otherwise irremediable growth.

3. In a considerable proportion of all cases, thymic growths display a tendency to confine themselves largely or even exclusively to the structures of the thoracic cavity where, however, their ultimate degree of destructivity is scarcely to be paralleled in the domain of neoplasia. Particularly note-

worthy is the propensity of such growths to destroy lung tissue either by compression or by direct infiltration, and to penetrate the pericardium and invade the heart muscle. In still other instances, in addition, secondary deposits are set up in extrathoracic tissues, notably by the perithelial sarcomata.

4. (*a*) In spite of the extensive local invasion and destruction of tissues produced by thymic growths, symptoms and signs of increased intrathoracic pressure are not uncommonly delayed for a long period of time—often months, sometimes, it is estimated, for a year or more. When such symptoms and signs finally assert themselves, however, they are apt to do so abruptly and to progress with astonishing rapidity, death occurring in a few weeks or months. It is a noteworthy example of the adaptability of mobile and compressible structures to the gradual encroachment of pressure and of the rapidity with which death occurs when the process of adaptation is exhausted.

(*b*) In a second group of cases, usually late in their course and in association with pressure signs, the thymic lymphosarcomata may suddenly commence to pour their lymphocytes into the blood, constituting an acute lymphocytic leucemia, in this manner terminating life. It need scarcely be pointed out that this phenomenon is limited to the lymphosarcomata and that leucemic conversion of the other malignant tumors and tumor-like growths of the thymus is unknown.

(*c*) A third and small, but extremely important group of thymic tumors is associated with the symptoms of myasthenia gravis. This remarkable alliance has been noted in about 20 per cent. of all cases of myasthenia gravis thus far investigated at autopsy. It occurs sufficiently often, however, to be sought for in every case and its detection is obviously important from the standpoint of treatment. The association in question is not limited to any single variety of thymic growth, but has been noted in simple hyperplasia of the thymus and in at least three widely divergent forms of thymic tumors, namely, lymphosarcoma, perithelioma and epithelioma. Its significance lies, not so much in the nature or geographical extent of the thymic lesion, as in the functional disturbances for which these lesions sometimes appear to act as sponsor.

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SUTURING WOUNDS OF THE HEART

By Daniel C. Elkin, M.D.

of Atlanta, Georgia

From the Department of Surgery of Emory University

The modern era of surgery of the central circulatory system began with the bold attempts of Farina,[1] Cappelen,[2] and Rehn[3] in 1895-1896 to suture wounds of the heart. It had been casually considered before this for Larrey[4] had successfully drained a hemo-pericardium, but in 1883 Billroth[5] made the ridiculous statement "that the surgeon who should attempt to suture a wound of the heart would lose the respect of his colleagues," and as late as 1896 Stephen Paget[6] stated that "surgery of the heart has probably reached the limits set by nature to all surgery; no new method and no new discovery can overcome the natural difficulties that attend a wound of the heart."

Since the occasion for cardiorrhaphy arises so rarely the surgeon must have in mind definite principles and methods rather than accept the curious statement of Sir Charles Ballance[7] that he should regard the suture of heart wounds merely as a part of the "day's work, and just as he plunges his hand into the abdomen into a mass of blood in a case of ruptured spleen or in a case of ruptured tubal gestation and seizes the bleeding spot, so he will now plunge his hand into the pericardium and seize the heart, and, by digital compression, control the hæmorrhage and proceed to suture the heart." That the mortality in the series of heart wounds reported in 1909[8] was 63 per cent. and 33 per cent. in the series reported in 1923[9] shows that a better technic was being evolved just as it has been in the operations for ruptured spleen and ruptured tubal gestation, since the "day's work" for a surgeon in 1909 differed little from that in 1923.

The object of this paper is to set out certain definite principles in diagnosis and treatment of cardiac wounds together with a technic of suture applicable to most cases. Two successful instances are shown. (Figs. 1 and 2.)

Diagnosis.—Every attempt at accurate diagnosis should be made before operation since exposure of the heart is in itself hazardous. However, if unable to determine for certain whether or not an injury exists, it is safer to do an exploratory pericardiotomy than to run the chance of death from heart tamponade or hæmorrhage. The position of the wound is of some importance in diagnosis, but the course of a bullet or even a knife thrust is notoriously misleading. Wounds just to the left of the sternum from the second to the fifth rib are the most apt to cause cardiac injury.

There is usually a history of freedom from any symptoms for five or ten minutes after injury, followed quickly by exhaustion and collapse. Bleeding is profuse at first and with the stage of collapse is checked. Both the collapse and the checking of the hæmorrhage are due to tamponade of the heart. The

patient is usually frightened, cold, clammy, and thirsty. The pulse may be weak or absent, and the arterial pressure lowered or imperceptible. The venous pressure is raised as is evidenced by prominent, strutted, external jugular veins. Röntgenogram of the heart is of no value since death may occur from a rapidly occurring tamponade from an amount of blood too small to cause a noticeable change in the size and contour of the cardiac shadow. The electrocardiogram is usually normal for several hours even though tamponade is present or even if a coronary vessel is severed. The main point in diagnosis is the recognition of tamponade of the heart from blood, thereby

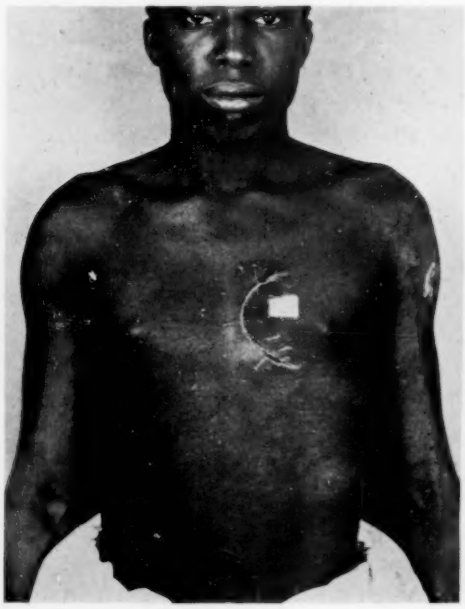

FIG. 1.

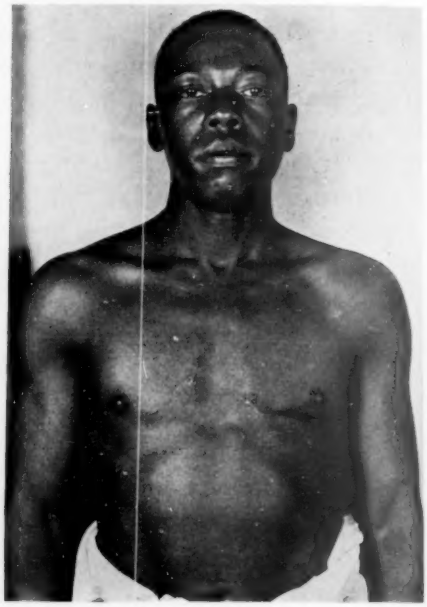

FIG. 2.

FIG. 1.—Patient two months after suture of wound of right ventricle. Exposure by skin and muscle flap and removal of three costal cartilages.

FIG. 2.—Patient two months after suture of wound of left ventricle. Exposure by transverse incision with removal of fifth costal cartilage and retraction of fourth and sixth cartilages.

raising the venous pressure by pressure on the vena cavæ, and lowering the arterial pressure by prevention of filling and therefore of emptying of the heart. The history of a symptomless interval, similar to that seen in intracranial hæmorrhage, during the time the pericardium fills with blood, is the most important point in the history.

Having established a diagnosis, immediate operation should be carried out. If the pulse is becoming weaker or is imperceptible and the arterial blood pressure is dropping, scrubbing the hands and the usual operating-room preparations should be dispensed with. The instruments may be sterilized by placing them in alcohol and the operator and assistants will save much valuable time by mere use of sterile gowns and gloves. The incision should be planned to secure the best exposure in the quickest time and with the least shock. The median sternotomy (Duval-Barasty), certainly gives excellent

exposure to all the heart and great vessels, but splitting the sternum requires a great deal of time, as does the closure of the wound, and is certainly productive of shock. It is mentioned merely to condemn it, since in cases of severe hæmorrhage or increasing tamponade, the patient would not likely survive. Operations should always be carried out on the left side even though the wound is to the right of the sternum. The position of the heart behind and to the left of the sternum makes exposure from the right side impossible. The intercostochondral thoracotomy (Spangaro), offers a rapid approach but not a particularly good exposure. It can be improved by removing one

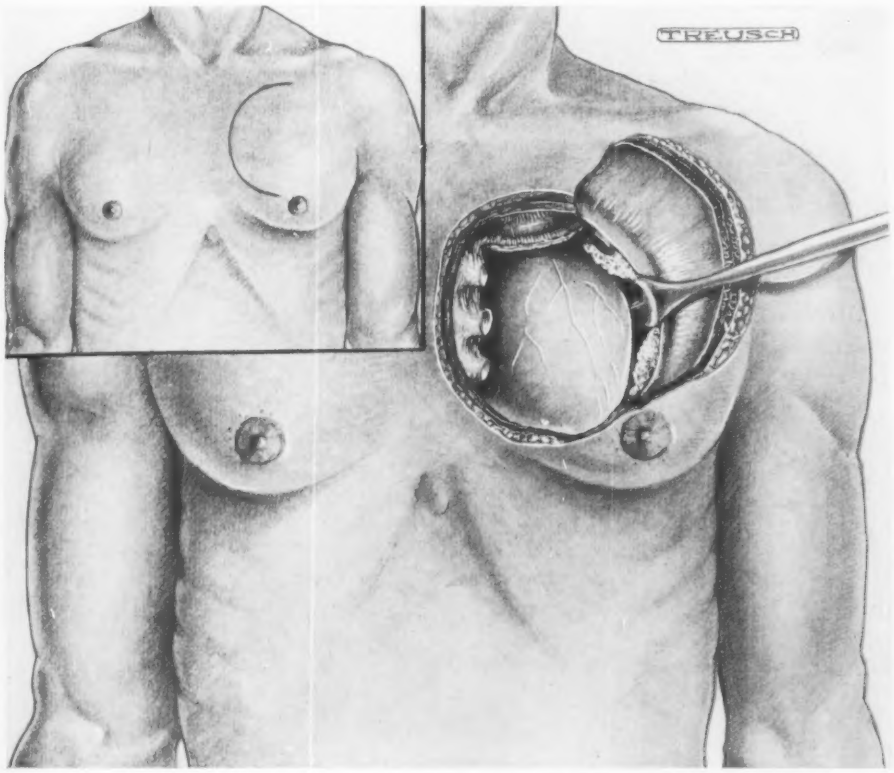

FIG. 3.—Method of flap exposure and removal of three costal cartilages.

cartilage through the transverse incision and spreading the cartilages above and below it.

A third method and one giving excellent exposure is as follows: under procaine anæsthesia, a flap of skin, fascia, and muscle is turned outward, exposing the third, fourth and fifth left costal cartilages and ribs. The cartilages are removed, taking care not to injure the underlying pleura, and the internal mammary vessels are ligated. The parietal pleura is then carefully displaced outward and the pericardium exposed. (Fig. 3.) The pericardial wound is then located and enlarged. If there is an appreciable amount of blood in the pericardium it will gush out on enlarging the wound,

and the contractions of the heart, being released from the tamponade, will increase in force. Should the heart be beating feebly, the tamponade should be immediately removed by passing a finger behind the heart and evacuating the blood and clots, and the heart stimulated by the injection of fifteen minims of 1-5,000 solution of adrenalin. The difficulty is in placing of the first hæmostatic suture, since with each heart beat the wound becomes obscured

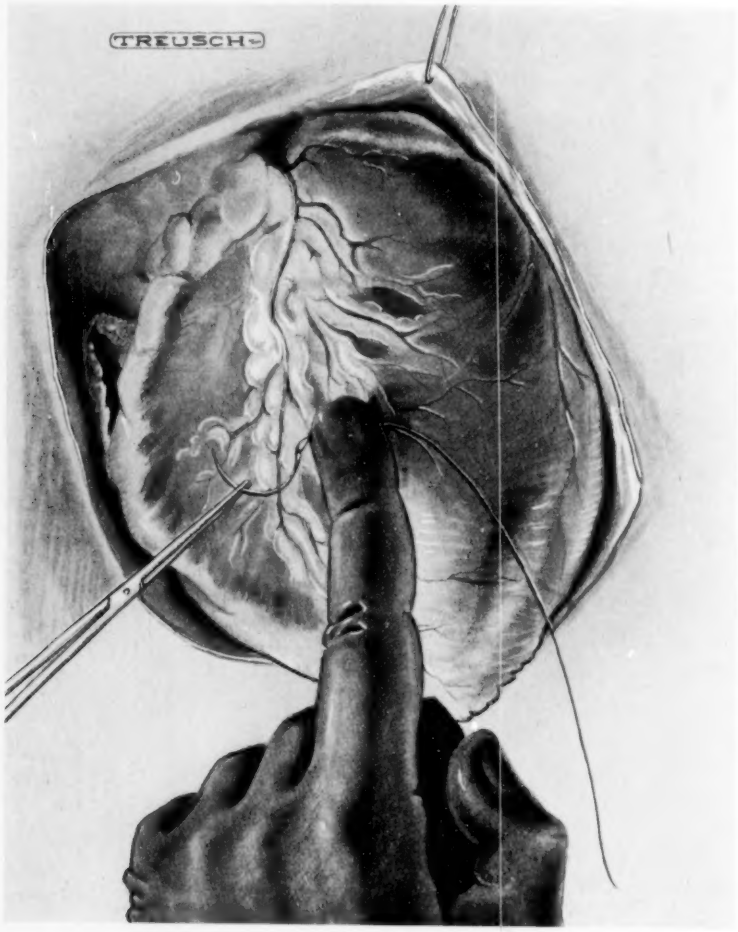

FIG. 4.—Method of controlling bleeding if wound is anterior and near the apex. The index finger of the left hand is placed on the wound and the suture passed through the wound under the finger. This suture is then used for traction and hemostasis until the other hemostatic sutures are placed.

with blood. If the index finger of the left hand is placed directly over the wound the flow will be stopped sufficiently long to allow the passage of a suture directly under the finger. (Fig. 4.) Fine black silk (size A) is the suture of choice. This is left untied and held in the left hand for traction and hæmostasis, and two or three other sutures can then be readily passed to completely close the wound. Under no circumstances should the finger be

placed *in* the wound, since the heart muscle is extremely friable and the wound will be immediately torn and enlarged.

Should the wound be located in an auricle, behind the sternum, or posteriorly, the method described by Beck[10] is the procedure of choice. He advocates the placing of a stay suture at the apex, and with this the heart can be moved for inspection and steadied during suture. "The apex suture is held under traction between the thumb and third finger of the left hand, and the index finger is placed on the wound." While this is an excellent procedure for wounds not easily accessible, it appears unnecessary where a suture can be as easily passed through the wound and be used for both traction and hæmostasis.

After control of the hæmorrhage the pericardium should be carefully cleansed with saline solution. Care should be taken not to handle or touch the pericardium except as absolutely necessary since after cardiac suture pericardial effusion invariably occurs. The muscle and skin are then closed with interrupted sutures, and a drain or soft rubber carried down to the pericardium to allow drainage of the effusion. This is removed forty-eight hours later.

CONCLUSIONS

(1) The necessity of cardiac suture arises so rarely that some definite method must be at hand if the procedure is to be successfully accomplished.

(2) A simple method of approach and suture is outlined.

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THE EFFECT OF ARTERIOVENOUS ANEURISMS UPON THE HEART

WITH THE REPORT OF A CASE STUDIED BY PROFESSOR RUDOLPH MATAS, DR. GEORGER HERRMANN, AND THE AUTHOR *

By Mont R. Reid, M.D.

of Cincinnati, Ohio

One of the serious consequences of arteriovenous aneurisms is the effect upon the heart. My interest in this subject began in 1914, during the course of some experiments which Dr. W. S. Halsted[1] and I were doing to determine the effects of metallic bands applied to blood-vessels. As a collateral branch of this study, we began producing arteriovenous fistulæ in dogs to determine their effect on the vessels. We were familiar with the fact that a large fistula between the aorta and vena cava might cause a sudden death of the dog and decided to watch the effect upon the heart of fistulas between smaller vessels. In the course of two to three years we were fully convinced that a fistula between the large vessels of the neck or legs may cause marked cardiac hypertrophy and dilatation and in some instances cardiac decompensation and death. This was shown by teleoröntgenograms of the heart, electrocardiograms and autopsies. During these experiments a study of fourteen cases previously admitted to the Johns Hopkins Hospital revealed a very high incidence of cardiac hypertrophy, dilatation and auricular fibrillation, especially in the long-standing cases. In one case, the heart was so bad an operation was not performed. The patient was forty-eight years old, and, although no cause could be found for the cardiac trouble, the aneurism was not suspected of having any etiological bearing. In the literature we found two cases (one axillary, the other femoral) which Osler[2] had watched for fifteen to nineteen years. They both died of heart trouble at the early ages of twenty-nine and forty-six years, without the aneurisms being suspected as the cause. I also learned that congenital or spontaneous communications between the thoracic aorta and vena cava usually led to marked cardiac disturbances, frequently sudden death.[3]

These observations led me[4] to report, in 1920, that I considered arteriovenous aneurisms a very definite cause of serious cardiac disturbances, which might be relieved or cured or prevented by curing the aneurisms. This statement has been abundantly substantiated by the clinical and research studies of Matas,[5] Holman,[6] Leriche,[7] Callander[8] and many others. Holman has produced cardiac trouble in dogs and has cured it by excising the fistula. Many observers have watched the heart of patients decrease in size by temporary occlusion of the fistula and have completely relieved damaged hearts by permanently curing the aneurism.

Before the Southern Surgical Association in 1923, Professor Rudolph

* Read before the Southern Surgical Association, December 8, 1931.

Matas[5] discussed the effects of arteriovenous aneurisms upon the heart and stressed the fact that the shunting of a large quantity of arterial blood into a vein increased tremendously the amount of work that the heart is called upon to do. Holman, in a series of careful experiments reported in 1923 and 1924, measured the cardiac output with arteriovenous fistulæ open and closed and demonstrated conclusively that the heart does handle an increased volume of blood while the fistula is open. His work has been amply confirmed by others. The amount of this increase is usually directly proportionate to the calibre of the vessels involved and the size of the fistulous opening. In a very recent study of a case which had had a femoral arteriovenous aneurism for six years, Carter Smith[9] showed a reduction of 58 per cent. in cardiac output and an increase of 122 per cent. in the coefficient of utilization of blood following the closure of the fistula.

As was originally shown by Carrel[10] and Bernheim, a large communication between the aorta and vena cava frequently so overloads the heart that sudden death occurs. Holman occasionally caused sudden death in dogs by the simultaneous production of bilateral fistulæ between the carotid arteries and external jugular veins. In those cases which do not result in a rapid or sudden death, such as when the aorta ruptures into the vena cava, the heart is permanently overloaded until death; or until the fistula is closed.

Although this effect of increasing the amount of blood that the heart has to handle in cases of arteriovenous aneurisms is definitely proven, it is probably not the only cause of cardiac trouble. Except in those cases of sudden death occurring immediately or soon after the production of the fistula, the effects upon the heart from a disturbance to the arterial side of the fistula must be considered. As has been shown by Lewis and Drury,[11] clinically, and by Gage and Herrmann,[12] experimentally, a large arteriovenous fistula produces, in effect, the hydrodynamics of aortic regurgitation. There result a lowering of the blood-pressures, especially the diastolic pressure; an increased heart rate, water-hammer pulse and capillary pulsation. This disturbance of pulse pressure is of special interest to me.

Thoma[13] advanced the idea that a normal pulse pressure is essential to the integrity of an arterial wall. Ney[14] showed that an exceedingly low pulse pressure obtained in the artery just proximal to an arteriovenous fistula, and it is our belief that this is largely responsible for the thinning and degeneration of the proximal artery. In many long-standing cases this vessel resembles more a dilated vein than an artery. It seems rather significant that when there is not a marked dilatation of the proximal artery it is rare to see any serious effects upon the heart. This local effect of a lowered pulse pressure is different from the generalized effect of a markedly increased pulse pressure. I am not prepared to interpret the meaning of these disturbances to the arterial side of an arteriovenous fistula but I cite them in support of my belief that they do play a very considerable rôle in the cardiac disturbances even though they are secondary to the effect of the increased amount of work by virtue of the short-circuiting of blood.

Effects upon the heart, ranging from symptomless slight cardiac hyper-

trophy to extensive cardiac decompensation, have been reported in association with arteriovenous aneurisms. The author[15] has reported a case in which the heart was so completely decompensated that the patient had general anasarca and had been bedridden for six months. During this time he had been treated for cirrhosis of the liver and had had numerous abdominal tappings with the withdrawal of many litres of fluid. The excision of the fistula relieved completely all symptoms and restored the heart to competency for normal work and exercise. Hoover[16] has reported a similarly striking case.

It would be of very little value to try to determine the incidence of cardiac trouble among the reported cases of arteriovenous aneurisms, for it is only recently that the causal relationship has been definitely established. Even with this knowledge the symptomless cardiac damage is easily overlooked without a careful study of the heart by means of teleoröntgenograms and electrocardiograms. That the great majority of arteriovenous aneurisms will sooner or later result in premature death from heart trouble is a fact, however, that should constantly be borne in mind. I am well aware that such a statement is not news to the members of this society. However, my experience leads me to believe that relatively few members of our profession at large possess this knowledge. It is with the hope that a more general dissemination of this effect of arteriovenous aneurisms may result that I take this opportunity of recording another illustration of it. I am particularly pleased to present the following case to this society before which Professor Matas has so often spoken on the same subject, for it is due entirely to his generosity in sending the case to me that I have it to report. In reality, I was only the technician. His exhaustive and accurate studies constitute the major portion of my story.

The case is that of a white man, aged twenty-five years, who had had a femoral arteriovenous aneurism for seventeen years. The communication was in the left thigh just below Poupart's ligament, almost at the exact level of the origin of the profunda femoris artery. (Figs. 1, 2, 3 and 4.) The condition resulted from a gunshot wound with a .22 rifle. For a great many years he carried on the usual work and play of youth without being conscious of any discomfort other than the noise of the aneurism and the increasing varicosities of the leg and groin. Within recent years he had been repeatedly told by physicians that his heart was greatly enlarged. He had become conscious of a disordered heart action; shortness of breath was beginning to be a handicap while exercising; the left foot felt cold at times and frequently "went to sleep"; cramps in the calf of the leg were common. He had learned that occlusion of the fistula by manual pressure made his heart feel better and his foot warmer. He had had no swelling of his legs and there was no history suggestive of a cardiac decompensation. He had not been at all incapacitated for work.

This patient consulted Professor Rudolph Matas, August 19, 1930, and I am indebted to him for the privilege of incorporating his studies in this report: Age of patient, twenty-four years; 5 feet, 8 inches tall; weight, 120 pounds. *Diagnosis.*—Arteriovenous fistula of common femoral vessels caused by bullet wound (.22 calibre rifle); inflicted sixteen years ago, when the patient was eight years old. The fistula is situated about one centimetre below Poupart's ligament at the base of Scarpa's triangle. In the course of the years that have followed the injury, great varicosities have developed in the saphenous and epigastric tracts. Typical systolic double murmurs can be heard at the vortex of

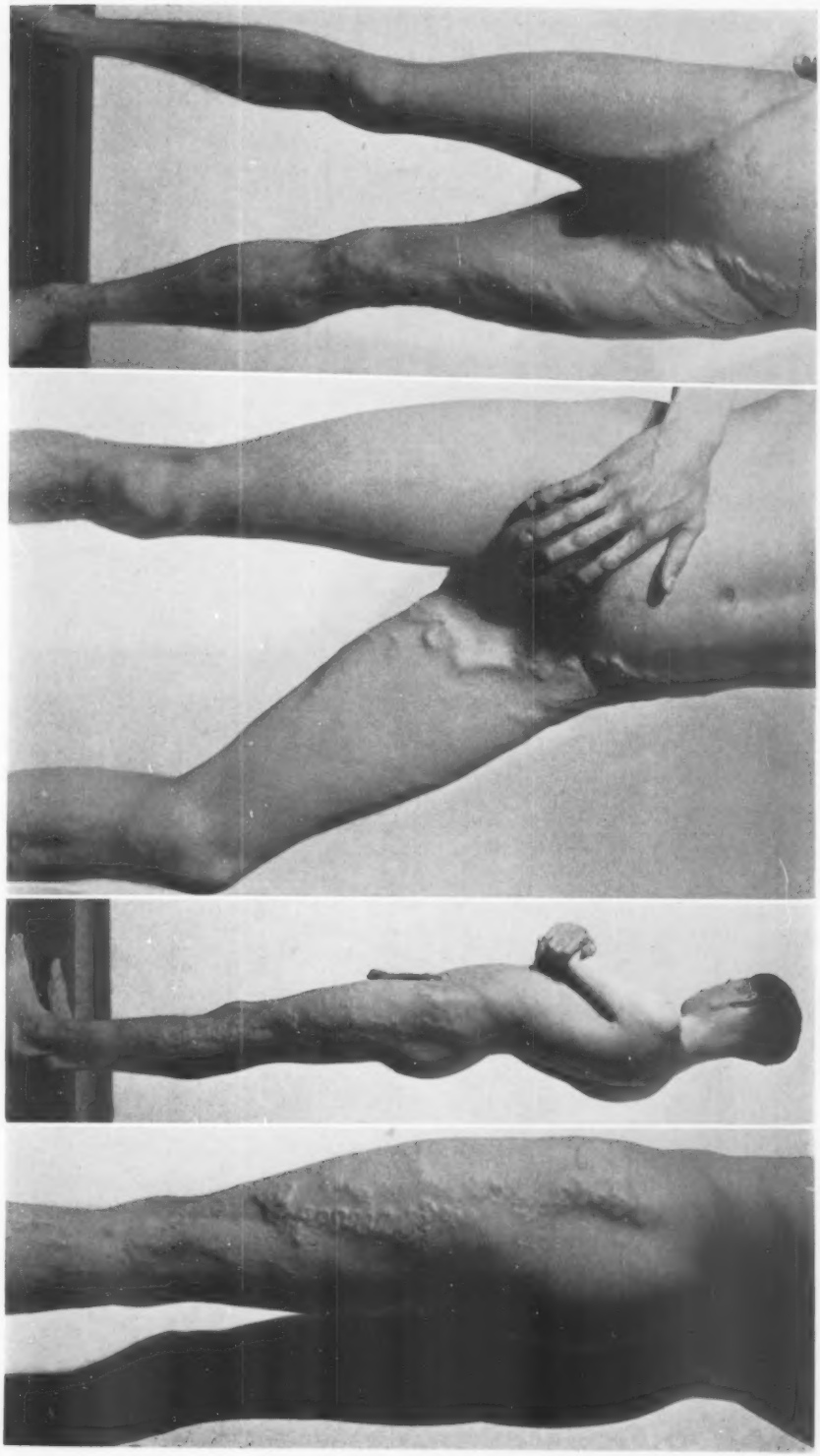


FIG. 1.

FIG. 2.

FIG. 3.

FIG. 4.

FIGS. 1, 2, 3 and 4 are photographs of the patient before operation. Note the dilated veins. They pulsated and carried a mixture of venous and arterial blood.

fistula, where the venous hum and roar can be heard with the greatest intensity. The thrill is felt below the fistula, as low down as the knee, and above along the iliac vein and vena cava to the level of the diaphragm. A faint murmur, but not a typical Makin's murmur, is present at the apex of the heart. The typical Branham[17] bradycardiac syndrome occurs on compression of the fistula—slow pulse and rise in blood-pressure. Pulse and heart-beat before compression, 84. Pulse and heart-beat after compression, 52. There is a marked Hill and Flack sign,[18] as shown by the differential blood-pressure. In the right arm, it is $\frac{119}{75}$ and rises to $\frac{125}{75}$ on compression of the fistula. In the right leg (calf), it is $\frac{165}{30}$ and rises to $\frac{170}{40}$ on compression of the fistula. In the left leg, without compression of the fistula, it is $\frac{75}{58}$. In the left leg, with compression of the fistula, a reading cannot be obtained. The peripheral pulses are faintly felt in the dorsalis pedis and post tibial vessels, disappear on compression of the fistula, but return on prolonged compression when the collateral circulation is well established.

The hyperæmia test shows a return of color, after application of the Esmarch bandage over the fistula, in three to five minutes.

The pyrometer was broken and no electrothermic tests were made.

The electrocardiogram confirms a prolongation of the diastolic pause, with an immediate restoration to normal on compression of fistula.

Professor Matas sent the patient to Dr. George Herrmann for a more complete study of his heart. The report of Doctor Herrmann is as follows:

The patient presents a picture of a long-standing left femoral arteriovenous aneurism with concomitant cardiac changes. It is an interesting fact that the patient had no complaints whatsoever until one shut off his aneurism, when he had a peculiar, short, tight, dyspnœic sensation in the chest. After one had done this several times, the patient said that he apparently became accustomed to it and had very little sensation when the aneurism was cut off by manual pressure. He had noticed a purring from the very time that he left his bed after the removal of the bullet. He has palpitation on excitement but apparently not on exertion. He has no dyspnœa under any of the ordinary circumstances and no other symptoms. He has had no œdema, no cyanosis, no syncopal attacks, and, in fact, nothing to suggest that he has had any impairment of his heart muscle.

The physical examination showed a very slight nodding of the head, slight throbbing of the carotid arteries and a considerable pulsation in the subclavian vessels. This was also palpable in the aortic arch of the substernal notch. His cardiac apex was considerably displaced and there was an area the size of a silver dollar in about the centre of the axillary line which pulsated with each rise of the apex. The point of mechanism intensity of the apex beat was apparently in the fifth interspace in the anterior axillary line, eleven and one-half centimetres to the left of the mid-sternal line. There was a shock with systole and a considerable heaving movement about the area. The cardiac area on percussion measured three and one-half to four centimetres to the right and fifteen centimetres to the left of the mid-sternal line. I could hear a systolic murmur over the base which was especially loud in the pulmonic area, and this disappeared entirely with the closing of the communication, just as you had observed. With the obliteration of the fistula, the pulse rate dropped from 88 to as low as 46 and the blood-pressure changed from 114/54 to 118/84. There were throbbing of the fingertips and capillary pulsation.

I made several electrocardiographical studies for long and for short compressions. A compression for one second resulted in a drop in pulse rate from 80 to 50 and the change in the diastolic interval, 0.24 second to 0.80 second and it took about fourteen seconds for recovery, but the diastolic interval of the last beat was 0.28 second. I thought perhaps it would be interesting to compare the varying lengths, so I shall enclose a table. (Table I.) One other effect noted in the electrocardiograms was the fact that the T-waves of auricular activity became much smaller and were almost erased during the period of compression. The X-rays taken before and after compression of the

fistula showed the distinctly enlarged heart to be reduced in size at least one centimetre. The films had not been measured when I saw them; I simply superimposed one upon the other.

Our own studies entirely confirmed those made by Professor Matas and Doctor Herrmann. In addition, we made a few observations which I shall include.

In the region of the fistula the veins can easily be seen to pulsate; the pulsation is felt as far down as the knee. These veins definitely carry a mixture of venous and arterial blood. In the prone position there is no collapse of the distended veins unless the fistula is compressed. When the leg is elevated to an angle of 90°, those of the leg slowly collapse while those in the groin and abdominal wall remain distended. The venous pressures were studied by Doctor Louis B. Owens, using the apparatus devised by Eyster.

TABLE I

Effect of Varying Intervals of Compression on Electrocardiographical Changes

Length of time of compression	36.3 sec.	17.46 sec.	2.56 sec.	2.4 sec.	1.36 sec.	3.2 sec.	3.3 sec.	3.3 sec.	3.14 sec.
Rate before compression	78	80	90	78	82.5	100	90	99	90
Diastolic interval before compression	0.27	0.24	0.14	0.26	0.24	0.12	0.14	0.14	0.12
Longest diastolic interval during compression	1.06 sec.	0.80	2	0.32	0.82	0.43	0.46	0.32	0.73
Rate during compression	46	50	78	65	45	75	72	50	48
Time of recovery	4	13.92	10.44	-	10.2	8.58	7.38	5.52	9
Recovery to diastolic interval	0.27	0.28	0.14	0.26	0.27	0.14	0.14	0.16	0.14

(1) With fistula open—in a large vein nearby, it is 60 millimetres of water. With fistula open—in a small vein nearby, it is 90 millimetres of water.

(2) With fistula occluded—in a large vein nearby, it is 60 millimetres of water. With fistula occluded—in a small vein nearby, it is 100 millimetres of water. Unfortunately, no venous pressures were taken after the operation.

The surface temperature in the thigh and particularly in the region of the aneurism is definitely elevated; below the knee it is lowered. The temperature of the foot drops very slightly after the application of a tourniquet to the thigh; following its removal there is no rise in temperature above its normal.

A faint pulse can be felt in the dorsalis pedia artery but none can be felt in the posterior tibial. After the fistula has been compressed for two minutes a definite pulse can be detected in both of these vessels, thus showing that there is a well-established collateral circulation.

The artery (femoral and iliac) proximal to the point of fistula is hugely dilated. The abdominal aorta appears to me to be considerably larger than normal.

Careful measurements of the legs do not reveal any lengthening or shortening of the

left leg as a result of the long-standing arteriovenous aneurism. This was also confirmed by X-ray pictures.

Repeated tests by the patient and by ourselves convinced us that he could easily withstand a permanent closure of the fistula. Between the time of Professor Matas' studies and ours, the patient had practiced occluding the fistula by pressure of his hand, and had reached the point where his heart felt better and he was definitely more comfortable when the fistula was closed. In Doctor Herrmann's studies it is noted that at the first closures of the fistula the patient experienced a "short, tight, dyspnœic sensation in his chest." With practice these sensations had disappeared, and, instead, he felt better the longer the fistula was closed.

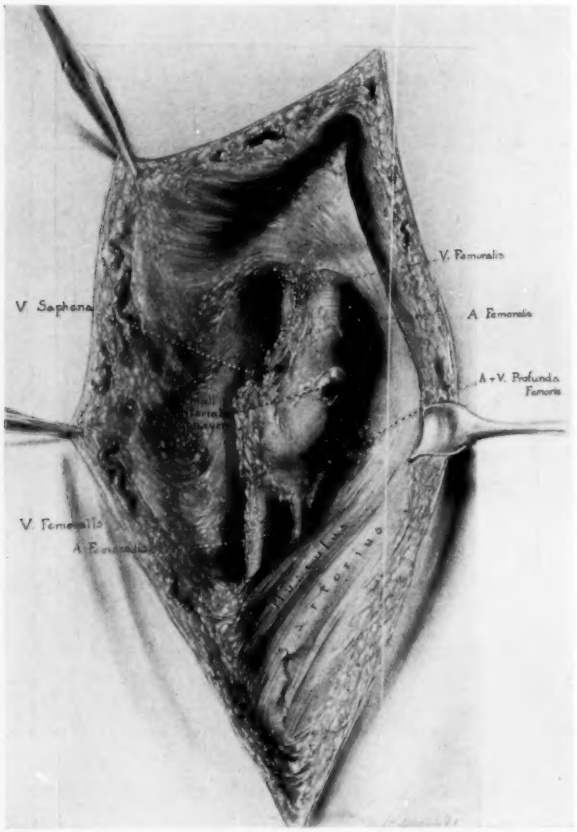


FIG. 5.—Illustration made at the time of operation. Note the large size of the proximal artery and the small arterial aneurism opposite the fistula.

Operation.—March 14, 1931. Anæsthesia: novocaine. Iodine and collodionized china silk technic was used.

Due to the location of the fistula, which was just opposite the opening of the profunda femoris branch, a rather large false aneurism (Fig. 5) where the bullet first penetrated the artery, the extensive scar tissue, and the extreme dilatation and thinness of the arterial wall proximal to the fistula, it seemed to me unwise to try to restore the continuity of the artery. Consequently, I excised the artery and vein as shown in the illustration (Fig. 6). At the beginning of the operation the patient's pulse rate was 84 per minute; at the completion of the operation, it was 64.

The operation was relatively easy and was accomplished without any difficulty with hæmorrhage. The wound was perfectly dry when we closed it. However, a fairly

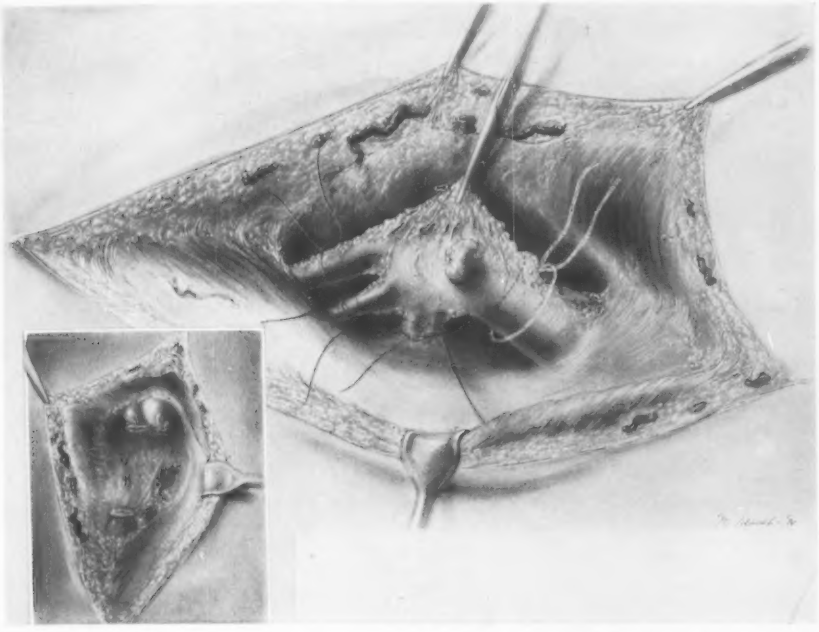


FIG. 6.—Arteriovenous fistula of femoral vein and artery.

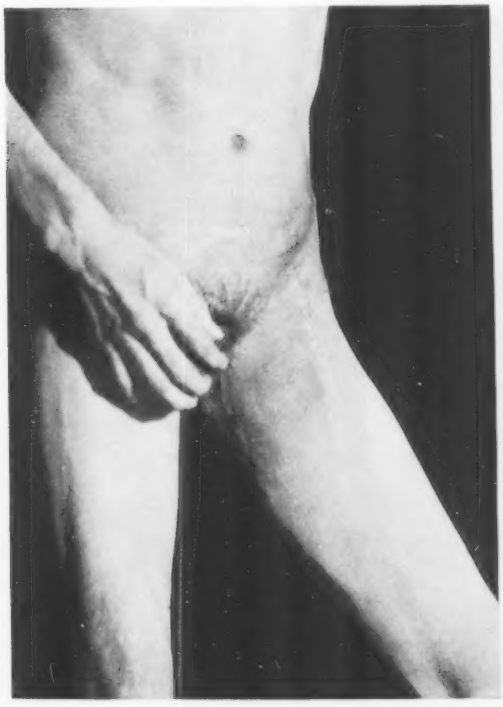


FIG. 7.

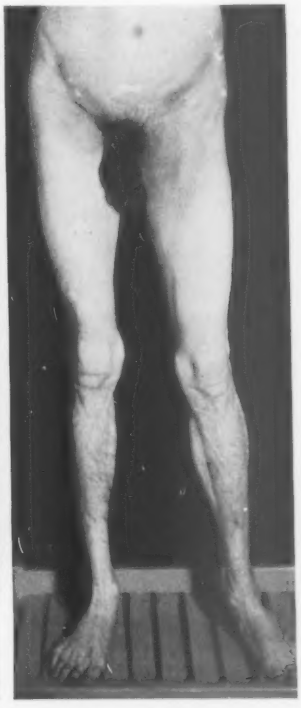


FIG. 8.

FIGS. 7 and 8 show the condition of the leg one month after operation.

extensive hæmorrhage occurred into the tissues on the second day after operation. This resulted in an extensive ecchymosis over the lower abdomen and upper thigh. The hæmatoma was absorbed and the wound healed *per primum* without our having to open

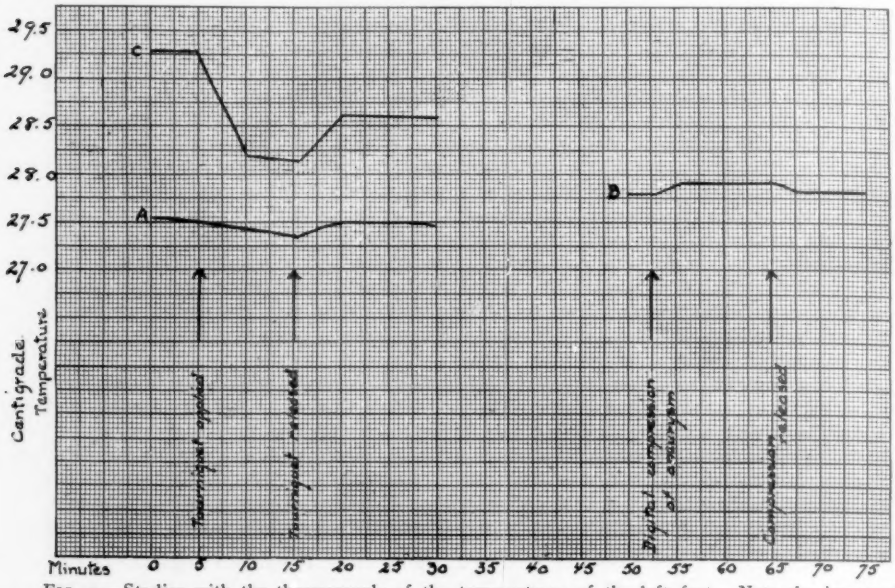


FIG. 9.—Studies with the thermocouple of the temperatures of the left foot. Note the increased temperature and the normal response to a tourniquet one month after operation. A—Before operation. B—With single compression of the fistula. C—One month after operation.

it. I am at a loss to explain this hæmorrhage unless it was due to a rupture of the vein-like arterial wall. All of the large vessels were transfixed and ligated with heavy braided silk. During the operation the diameter of the proximal artery was noted to be seven-eighths inch; of the distal artery, about one-quarter inch. After removal of the

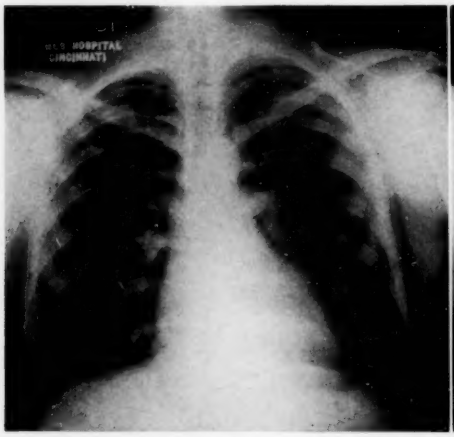


FIG. 10.

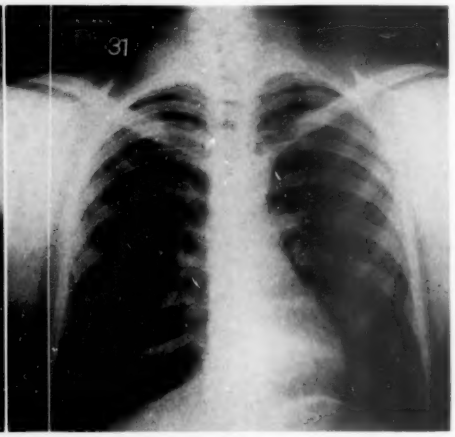


FIG. 11.

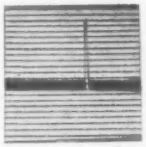
FIG. 10.—Teleoröntgenogram of the heart before operation.
FIG. 11.—Teleoröntgenogram of the heart one month after operation.

aneurism the communication between the artery and vein measured about three-eighths inch in diameter. The wall of the proximal artery was noted to be very thin and like that of a vein.

At the completion of the operation a pulse could be felt in both the dorsalis pedis

and posterior tibial arteries. (Figs. 7 and 8.) This pulse remained palpable throughout his convalescence, although at times it was very faint. The left foot felt considerably warmer than the right for about ten days after the operation. The pulse rate, which was between 80 and 90 before the operation, dropped to 64 immediately after the operation, rose to 80 on the third post-operative day, and then dropped to 70 on the fifteenth day and remained at about this level until the time of his discharge from the hospital.

Both feet were studied by means of the thermocouple (Fig. 9) before the operation and twenty-seven days after it. The right foot gave a normal response in temperature on both occasions following the application of a tourniquet. The left foot, before the operation, showed almost no decrease in temperature following the application of the



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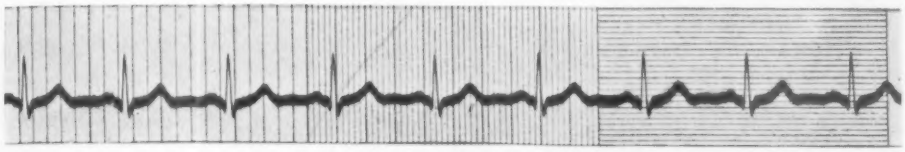
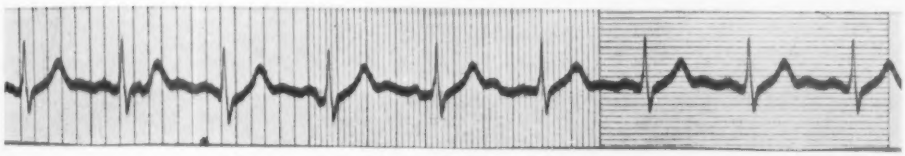
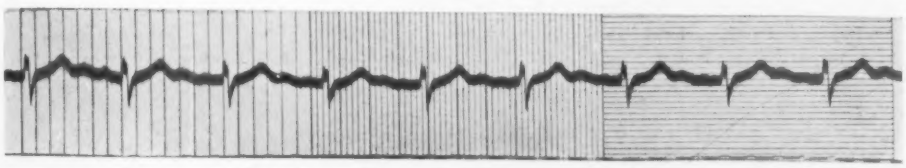


Lead No. 1.—Between Right and Left Arms.



Lead No. 2.—Between Right Arm and Left Leg.



Lead No. 3.—Between Left Arm and Left Leg.

FIG. 12.—Electrocardiogram made before operation.

tourniquet, while twenty-seven days after the operation it had risen two degrees Centigrade in temperature and gave the normal response to the use of a tourniquet.

Twenty-seven days after the excision of the aneurism the size of the heart was very appreciably decreased. (Figs. 10 and 11.) The retrosternal width at the level of the second ribs was 4.7 centimetres; the greatest diameter was 11.5 centimetres. Before the operation the corresponding measurements were 5.2 centimetres and 14.5 centimetres. The decrease in size of the heart after operation is most strikingly illustrated in the prints of the teleoröntgenograms, which were made under exactly the same conditions.

Electrocardiographical Studies.—Dr. Johnson McGuire very kindly furnished me with the following data and comments.

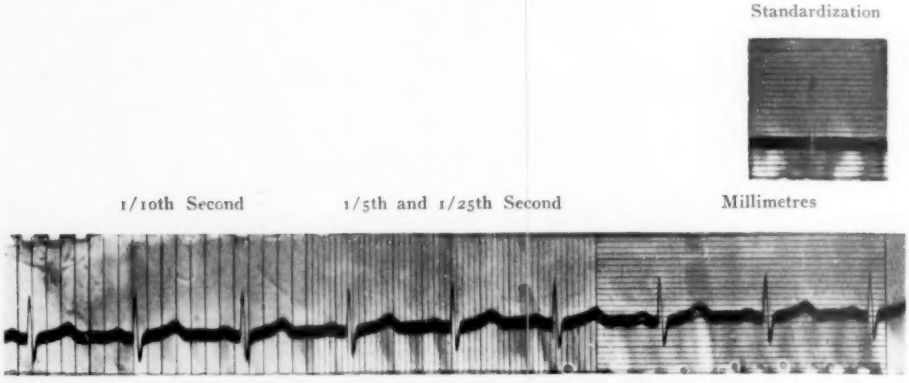
(A) *Before Operation.*—(Fig. 12.) Sinus arrhythmia; tendency to left axis deviation; U-waves present in leads 2 and 3; P-waves abnormal in all leads; diastolic pause 0.22 seconds; rate 90; T-waves measure in lead 1, 2.0 millimetres, lead 2, 3.5 millimetres, lead 3, 2.0 millimetres. (B) *After Operation.*—(Fig. 13.) Essentially normal; no tendency to axis deviation; slight sinus arrhythmia; diastolic pause 0.20 seconds; T-waves

lower voltage (lead 1, 1.5 millimetres, lead 2, 1 millimetre; lead 3, isoelectric) than in the pre-operative records; P-waves notched in all leads.

There is a relative shift of the electrical axis to the right when compared with the pre-operative records. The T-waves are of lower voltage.

SUMMARY

(1) Attention is again called to the fact that arteriovenous aneurisms involving large vessels usually affect the heart. The main factor in the causation of the damage to the heart is the increased amount of blood that it has to handle. This results from the quick shunting of a large amount of arterial



Lead No. 1.—Between Right and Left Arms.

Lead No. 2.—Between Right Arm and Left Leg.

Lead No. 3.—Between Left Arm and Left Leg.

FIG. 13.—Electrocardiogram made one month after operation.

blood back to the heart. Another factor which is probably of importance is that there results a condition resembling aortic insufficiency, although the lesion may be far removed from the aortic valves.

(2) A case of femoral arteriovenous aneurism, which had been present for seventeen years, is recorded. It illustrates many of the effects of this condition—cardiac hypertrophy and dilatation, Branham's bradycardiac phenomenon, disturbances of blood-pressure (Hill and Flack sign), changes in the electrocardiogram, pulsating varicosities, dilated and atrophied proximal artery, capillary pulsation, very adequate collateral circulation, *etc.* Excision of the aneurism relieved completely all cardiac symptoms and caused the heart to return to a normal size.

(3) This case strongly supports Professor Matas' teaching that the heart should be prepared for the complete closure of the fistula by a preliminary period devoted to temporary occlusions of it. Although the abundant collateral circulation reduces to a minimum the danger of peripheral gangrene, the heart should be considered and partially adapted to the great and sudden change which will follow the operation. An intelligent patient who has practiced temporary occlusion of his own fistula is usually quite certain when it can be permanently occluded without causing any cardiac distress.

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CANCER OF THE COLON AND OF THE RECTUM

PERSONAL EXPERIENCES FROM 1892 TO 1932

By Joseph Colt Bloodgood, M.D.

of Baltimore, Md.

Dr. T. S. Raiford (J. H. H., 1930), the Halsted Fellow in Surgery in the Department of Surgery of the Johns Hopkins University, and a special research student in the Surgical Pathological Laboratory of the Johns Hopkins University, has made a restudy of the records, pathological material, and final results of all the cases of cancer of the colon and rectum in the laboratory since the beginning of the Johns Hopkins Hospital in 1889.

We were very much helped by the first complete investigation by Dr. Paul Preble, in 1907, when a student of the medical department of the Johns Hopkins University. Unfortunately, the work of Doctor Preble was not published, as he could not finish it. Doctor Raiford's studies are in preparation for publication.

The subject was selected by me chiefly, because, from my own recent experience confirmed by Doctor Raiford's investigation, there are still unsettled problems in the operative technic of resection and the type of suture, especially when the cancer is situated in the transverse colon or rectosigmoid colon.

In addition, these studies demonstrate the importance of the gross and microscopical pathology of each individual case and the fact that the record of each individual case is of little value except for the study of post-operative mortality, unless the patient is traced up to the time of death or is known to be well five or more years after the operation.

The study of these records again demonstrates one of the fundamental facts in the clinical research of cancer cases, and that is: *The ultimate cure depends chiefly on the stage of the local malignant disease at the time the operation is performed.*

It also shows clearly another fundamental fact: The surgery of cancer was conceived and developed when the majority of cases of cancer came into the hands of operators when the local disease had become practically inoperable. Nevertheless, these early pioneers were able to demonstrate the truth of their conceptions of the proper operative technic, because, largely on account of accidental factors, patients came under observation first in operable stages, although still incurable on account of metastasis, and later in the operable and curable stage.

When I became associated with Doctor Halsted in 1892, one year after my graduation from the University of Pennsylvania, Billroth, of Vienna, had established the surgical technic of resection of the stomach and the suture of

end-to-end and lateral anastomosis, and Kraske,* in 1885, had ranked with Billroth in his contribution to the technic of resection of the lower end of the rectum, and had discussed the difficulties of the approach to the removal of cancer in the rectosigmoid colon too high for removal from below through the huge sacral wound made possible by the removal of the coccyx and a small piece of the sacrum.

William J. Mayo, in 1912, gave the best review of the literature of the surgery of the rectosigmoid colon from the time of Kraske to the date of his article. The majority of contributions since 1912 have had largely to do with substitutes for the Kraske operation and the safest handling of cancer in the rectosigmoid area.

Brief Historical Review.—When I entered the surgical clinic of Doctor Halsted, in 1892, there were a number of cases recovering from the Kraske operation for cancer of the rectum. One of them I was assigned to dress. This patient belonged to the operable, but incurable group on account of metastases. He lived almost four years in comfort and died of metastasis to the liver, after an illness of less than two months.

The first operable cancer of the rectum, therefore, occurred about 1892. The first operable cancer of the colon was situated in the sigmoid, was resected with successful end-to-end suture by Doctor Halsted in 1902, lived six years and died of metastasis to retroperitoneal glands. The first cancer of the rectum to be cured permanently by a complete Kraske operation was in 1900. This patient lived to a good old age until 1929. Within about three years after operation almost complete control of defecation was accomplished. She wrote me somewhat as follows: "You will be glad to learn how well I am. I am not only able to go to church, but to sit with comfort and without fear of an accident through my husband's sermons, and he has a reputation for being a 'long' preacher." This fortunate result in function after a Kraske resection is noted by Kraske himself in 1885 and all the literature since then.

I am not sure that any of the so-called modifications of the Kraske operation in the management and formation of the sacral anus have much to do with the improvement in function beyond the fixation of the lower end of the rectum, so that there is no prolapse of the mucous membrane, and the surrounding skin heals so that it reduces the actual opening into the bowel. I have frequently seen this take place when the entire healing was by granulation. Apparently good function is more a matter of luck than of management after this operation.

* In Kraske's article in the Archiv. für klinische Chirurgie, vol. xxxiii, pp. 563–574, 1885, he pictured a technic of the complete excision of the rectum for high carcinoma in which he removed the coccyx and a piece of the sacrum, all the glands, and usually opened the peritoneal cavity and brought down the sigmoid and fixed it in the sacral wound. In my opinion, Kraske's relation to the complete operation for cancer of the rectum is the same as Halsted's complete operation for cancer of the breast, Billroth for resection of the stomach, and Wertheim for the radical operation for cancer of the cervix.

There seems no question as to the explanation of the larger number of cures after resection for cancer of the left colon, especially of the sigmoid, rather than of the right colon, especially of the cæcum, which is most accessible. In the earlier years, it was obstruction—and usually acute obstruction—that brought the patient to the surgical clinic. The first operation was colostomy, the second resection. The explanation of this is that the fecal matter in the left colon is solid and in the right colon, especially the cæcum, liquid.* The first permanent cures after the complete resection of the right colon for cancer of the cæcum were accomplished in 1910, eight years after the first five-year cure, in 1902, of a cancer of the sigmoid. The first permanent cure of a left-sided cancer of the colon was in 1904.

When one studies critically the records, the fact that strikes one first is the large per cent. of clinically inoperable cases, the small per cent. of cases in which any attempt was made at an exploratory laparotomy or an operative investigation of the cancer of the rectum, and the very slow progress of cases in which the local growth could be removed. In these so-called operable cases, in the beginning, among those who survived the more extensive operation, practically all died of metastasis to neighboring glands or remote organs within five years. Then there were a few who lived more than five years and still died of metastasis. There was nothing in the clinical history, except a slightly earlier intervention that differentiated the operable cases in which the patients survived ten to thirty years, from the operable lesions who died within ten years of metastasis. Even when we studied the microscopical pathology of the cases that died ultimately of internal metastasis from those who lived more than ten years and had no symptoms of metastasis when they died, we cannot always distinguish the cured case from the morphology and arrangement of the cancer cell. If the neighboring lymphatic glands in cancer of the stomach, colon and rectum are microscopically involved, there is rarely a permanent cure, although there may be a few temporary cures of five or more years. Now that cancers of the stomach, colon and rectum are coming under observation more frequently in the earliest stages of the disease, that is, within the shortest interval of time after the first symptom, we are more frequently able to grade the malignancy of the local growth and pick out those whom we expect to die shortly of metastasis. There seems no question that in the earlier years these grade III and IV tumors either died of metastasis without entering a surgical clinic, or were so distinctly inoperable when they entered the clinic that no tissue was obtained.

In addition to a great increase in the number of early cases of cancer of the colon and rectum, we are beginning to observe, as we also do in the stomach, more benign lesions, most of which suggest that they are the local lesion

* Doctor Raiford agrees with me that obstruction is a more common symptom in cancer of the left colon, especially in the region of the sigmoid. He also agrees with the fact that the fecal material is more solid in the left colon. He, however, suggests one other factor, decrease in size of the lumen of the colon, and reminds me that William J. Mayo has called attention to this factor.

that precedes cancer. The majority of these are papillomas, usually single. There is another remarkable suggestive observation—as the number of cases of cancer of the colon subjected to operation in the very earliest stages increases and the number of those who live five or more years also increases, we observe, first, that after three to five years more patients return with cancer in some other part of the colon. In my first case the malignant tumor first removed was situated in the rectosigmoid colon. The method was by the abdominosacral route, or the so-called combined resection, and a very fortunate recovery followed an end-to-end suture in the sacral wound from above and the placing of the anastomosis extraperitoneally by the suture of the peritoneum in the floor of the pelvis to the mobilized sigmoid colon above the suture line. This patient made an excellent recovery and nine years later survived a resection of the right colon for a chronic obstructing cancer of the ascending colon. Unfortunately, he succumbed to a chronic nephritis some six or eight months later. Then we began to observe patients returning at different intervals with benign polypoid tumors. This has occurred most frequently on the left side in the region of the rectum, rectosigmoid and sigmoid colon.

On a few occasions, in resecting a distinct cancer of the colon, we would also observe and remove a benign polypoid tumor.

This brief historical review is given chiefly to indicate that at the present time the most important factor in increasing the number of benign lesions of the stomach, colon and rectum and of operable curable lesions, rests upon educating more and more people to the protective value of selecting a physician while they are well and—perhaps just as important—seeking the advice of this selected physician while well, cultivating the habit of periodic surveys and—even just as important—seeking the advice of that physician the moment there are any signs or symptoms which were not present at the last preceding periodic examination.

My more recent studies, in spite of adverse opinions of many of my colleagues, indicate that the chief cause of the failure to cure cancer today cannot be placed on the fact that the first physician failed in making the proper examinations or failed to refer the patient to a physician who could make it. Undoubtedly, this factor is present, but it is not the chief factor.*

It is quite true that many surgeons with insufficient experience in the resection and suture or in the entire management of the pre-operative, operative and post-operative care of lesions of the stomach, colon and rectum, reduce the chances of their patient's permanent cure by too high an operative mortality. But this in itself is not a significant factor as compared with the

*Doctor Raiford agrees that in all the old histories and in many up-to-date ones the chief factor in late or inoperable cancer is that the patient delays in seeing any doctor. He also calls my attention to the fact that even today among the internes in the hospital wards rectal examinations are still neglected. In my clinic I am seeing more and more patients who have reported to their family doctor at once after the first symptom and their physicians have made the proper rectal examination or referred their patient to one more familiar with the diseases of the colon and rectum.

fact that the patient neglects periodic examinations and procrastinates from ignorance or fear or embarrassment when the first symptoms appear.

Clinical Features.—The vast majority of patients with single or multiple tumors of the colon, including the rectum, or with the earliest stage of a local growth which has assumed a malignant character, have definite warning symptoms of sufficient character—providing the individual is properly informed, has already selected his family physician and has had at least one diagnostic survey—to give him ample time to be examined when the disease is either still benign or in the operable curable stage. Neither the profession nor the public realizes or subscribes to the truth of this statement.

The warning most readily recognized is blood in the stools. Then there are repeated attacks of colicky pain, with and without diarrhœa or blood in the stools, with no explanation, such as indiscretion in diet. Then there is a sudden or gradual constipation requiring cathartics; unusual vague sensations within the abdomen; discomfort from tight clothes or belt when bending over. Everyone seems aware of the symptoms and an increasing number are being informed of the importance of these warnings. Obstruction is a late symptom. On the left side, especially when the lesion is in the sigmoid, this obstruction may appear early enough to save the life of the patient. It never does so when the malignant tumor is on the right side. Cancer in the mid-transverse colon* may cause only gastric symptoms. In one of my cases the gall-bladder was first drained for the symptoms. Three weeks after operation there were recurrent symptoms. The clinical picture impressed me as one of pancreatitis. When I explored the abdomen, there was no fluid and no fat necrosis. When I lifted up the omentum to examine the pancreas I found an annular obstructing mass, small in size, in the transverse colon. It was immediately resected to be followed by an end-to-end anastomosis. The patient lived more than fifteen years and died of other causes. One could write pages on the slight variations of the warnings or the symptoms described by these patients. It seems unnecessary and not helpful, at least as yet, to attempt to classify them. Cancer students all know that there is no difference between the warnings of a local lesion not cancer and a local lesion not cancer but which ultimately will be cancer—for example, a polypoid growth—and the local lesion which is cancer. This is fundamental for a local lesion in any part of the body, external and internal. It is this that makes differential diagnosis difficult in spite of modern diagnostic methods. It is the possibility of cancer that urges the necessity of periodic examinations and a thorough examination immediately after the first warnings.

* Doctor Raiford asks me why cancer of the colon may often have gastric symptoms only. He is inclined to explain it by the fact that the tumor itself in cancer of the transverse colon may involve the stomach. I have just read two histories in which the cancer of the colon was confined to the colon only; in addition, there was no hydrochloric acid in the gastric juice. He will go into this in detail in this paper. Therefore, it is always a good plan when the stomach is explored for gastric symptoms to examine the transverse colon, and *vice versa*. It would be difficult to distinguish colic in the transverse colon from colic in the stomach, and gastric secretion is very much influenced by pain.

Routine Examinations.—The chief risk lies in curtailing the examination, or stopping the moment something definite is found. Remember, lesions of the colon may have only gastric symptoms and now and then gastric lesions may have symptoms referred to the lower abdomen. Very frequently, lesions of the gall-bladder have no distinct signs or symptoms referred to the right upper quadrant. The examination should begin with a rectal examination in men during which the prostate should not be overlooked; in women, combined with a pelvic examination. In both, proctoscopical inspection should follow. The sequence of the fluoroscopical study and X-ray films of the colon after bismuth by enema and investigation of the œsophagus and stomach with fluoroscope and plate, and examination of the gall-bladder, and a plate of the abdomen for stone in the kidney or elsewhere, varies with the clinical picture. There is the least danger of overlooking a lesion or coming to an erroneous conclusion when the gastro-intestinal study is complete. For example, here is a case diagnosed and treated for gastric ulcer, when there was really a stone in the right kidney. Here is another where the diagnosis of cancer of the transverse colon was made from one picture after a bismuth enema. The surgeon who explored failed to find a cancer of the colon, but on account of induration of the pancreas naturally concluded that there was a cancer of the pancreas, and as there was no jaundice, did nothing. The patient died five days after operation from hæmorrhage. The autopsy revealed a non-malignant ulcer of the duodenum.

Even in the most experienced hands, it is often difficult to carry on a complete pre-operative investigation, and often operation is decided against without such a complete study.

Can a routine complete examination overlook a cancer of the colon?—Yes, when the lesion is situated above or beyond the visibility of the proctoscope. In some instances, it is justifiable to explore the colon, just as we explore the appendix, on the clinical picture only. The danger of overlooking a cancer of the stomach is much less. Balfour told me that they had one case in The Mayo Clinic during a visit some years ago. I have just had my first personal experience. Two of my associates, independently, after a complete gastro-intestinal study, rendered negative reports. Three months later the reports were positive. An operation confirmed the correctness of the second diagnosis.

I am gradually coming to the opinion that it is not an unnecessary precaution to make a complete gastro-intestinal study in a diagnostic survey or as a part of a periodic examination, even when there are no abdominal symptoms, just as I think it is a good plan to use the electrocardiogram as part of a complete diagnostic survey or periodic examination when the ordinary physical examination of the heart is negative. We do not now depend upon the physical examination of the chest alone; we always take an X-ray of the chest, or should do so.

Recently I made the statement in a number of my publications that it would add to the value of an investigation by a urologist to use the proctoscope. The same is true of the pelvic examination of women.

To increase the number of cures of cancer of the rectum and colon, we must give proper information to more people—persuade the medical profession to make more complete examinations. The evidence before me suggests that this is really more important than the reduction of the operative mortality. This mortality is relatively low in operable lesions, except after operations in the rectosigmoid area, which is high even in the most experienced hands. I am of the opinion that when a surgeon of less experience finds such a tumor in the examinations and there is no urgency on account of obstruction, he should refer such a case to a surgeon of much larger experience. As a matter of fact, they are well known and easily gotten at.

When such an unfavorably situated lesion of the colon is discovered at the exploratory laparotomy for obstruction, my advice is to do an appendicostomy which relieves the obstruction at once and leaves the operative field intact for the more experienced operator. If a colostomy is to be performed, it should be made high, at the junction of the sigmoid and ascending colon.

Intestinal Suture.—I was quite familiar with Senn's experimental work on end-to-end and lateral anastomosis with the decalcified bone plate when I was a pre-medical student at Wisconsin. At Pennsylvania, in the physiological laboratory of Professor Reichert, my classmate Hillier and myself performed many intestinal sutures of all types, using rubber bands instead of decalcified bone plates. However, never before my visit to Johns Hopkins, in 1892, did I see an intestinal suture performed on a human being. My first introduction was a gastroenterostomy for cancer done by Professor Halsted. He used the posterior route, retrocolic, a rather long loop. He used a single row of mattress sutures. His operation was entirely based upon his remarkable experiments on dogs. This work was done in Welch's pathological laboratory between 1884 and 1889, previous to the opening of the hospital. I know of no more perfect piece of anatomical work than this of Halsted's. It was he who demonstrated the value of the submucosa; he objected to the Lambert stitch, because it did not catch the submucosa. I am inclined to think that Lambert did catch the submucosa, but that he did not know it.

However, the great and dominating publication was that of Billroth, before 1885; that was shortly before Halsted's work. The English-reading student depended upon the Sydenham translation and the remarkable illustrations. These pictured the end-to-end anastomosis and the three rows of single interrupted silk sutures, the inner including the mucous membrane, the two outer not including the mucous membrane. Billroth made no mention of the value of the submucosa. He also pictured and described gastroenterostomy. Later Kocher developed his method of end-lateral suture after resection of the stomach. Then there were various changes in gastroenterostomy, anterior and lateral, with the final development of the Polya suture. Finney's remarkable pyloroplasty was developed before and after 1900. He accepted Halsted's mattress suture, did not employ a mucous-membrane suture, but did not depend on one row only.

What I want to emphasize is this: Intestinal suture was really established by Billroth. Certain details were later learned, especially in the suture of the large gut, which is more difficult than the small gut or the stomach. The difficulty in the suture of the large gut is that its circulation is not so good as that of the stomach or of the small gut, and the danger of perforation is due more to necrosis than the faulty suture. End-to-end anastomosis is more difficult in the colon than in the small intestine or between the duodenum and the stomach. The majority of operators have returned to the Billroth I operation on the stomach, which is an end-to-end anastomosis, but the majority of the same operators prefer the lateral in the small and always in the large intestine.

It has always been my opinion that operators, not only in their experiments on animals but in the actual operative technic on the human being, have exaggerated the danger of leakage. My great chief, Halsted, up to the time of his death, was working on dogs for a successful aseptic suture and he left us the remarkably conceived buttress suture, which is rarely employed even by his associates. It would appear to be chiefly applicable for end-to-end suture in the bottom of the pelvis after the resection of a rectosigmoid lesion. From my experience, it is less difficult to do the suture with ordinary small clamps without the more difficult measures as originated by Halsted. However, this still must remain a personal question with the operator. The extra danger in the most expert and experienced hands of resection and end-to-end suture of a cancer of the rectosigmoid area is so great in some cases that it seems wiser after resection to invert the lower end, close the peritoneal cavity over it, and do a high colostomy. My first successful case was in 1904.

Mikulicz' Method.—Many experienced operators even today, including Rankin, of The Mayo Clinic, follow this safer procedure in some cases of cancer of the colon. It adds unnecessarily to the time in the hospital and to the discomfort of the patient, and should be done only as a life-saving procedure.

In 1909 (ANNALS OF SURGERY, vol. lxix, p. 161, February, 1909), I reported and illustrated a modification of Mikulicz' method and a modification of the lateral anastomosis between the ends of the colon after a resection of a piece of the colon. (Figs. 17, 18, and 19.) The first operation by this technic was performed in 1906, and has been done on frequent occasions since.

The object of this suture is to prevent danger should there be a leakage in the inserted end of the large intestine. Every operator has experienced this distressing post-operative occurrence, which practically always ends in death. With few exceptions, the ends of the colon after resection can be brought together in this way and sutured into the peritoneal wound so that if any leakage takes place it will drain extraperitoneally. At my last resection a few weeks ago of a cancer of the transverse colon there was sufficient colon to allow any method of suture. There was a great temptation to do an end-to-end anastomosis. The patient had had no obstruction and the pre-opera-

tive preparation had been complete. The colon was empty. The patient was in good condition. Nevertheless, I chose the safer suture, as there was no tension. The only variation in technic was the employment of continuous catgut through the mucous membrane. The inversion was made with two rows of fine black silk. There was leakage on the tenth day, but the external wound had been drained. This complication prolonged the convalescence but the time was much shorter than if I had used the Mikulicz method.

Method of Inversion of the Colon.—When one resects the small intestine and decides on a lateral anastomosis, the ends of the small gut can be ligated with catgut and inverted with interrupted sutures of fine black silk. Some operators use catgut throughout. This method is not safe for the colon. The mucous membrane may not be properly caught by the ligature. It is my method to leave the small clamp on, close the mucous membrane with interrupted fine black silk, then place the first row of sutures through the wall of the gut over the clamp, withdraw the clamps, and invert the mucous-membrane row and then place at least a second row of fine black silk.

Resection of Cæcum and Right Colon.—Halsted, in 1893, resected a piece of ileum and cæcum, brought the two ends out and sutured them in the wound, but the patient died some weeks later and the autopsy showed cancer throughout the abdominal cavity. In 1894, Finney resected the ileum and a portion of the cæcum for a tumor in the ileocecal valve, producing chronic obstruction. He then made a lateral anastomosis. There was a leakage from the inverted end of the large gut, but fortunately it escaped extraperitoneally and the patient recovered. This patient was followed for more than twenty-five years. The tumor, however, proved to be benign.

Before I had my first resection for cancer of the cæcum in 1911, I learned from Dr. William J. Mayo his method of mobilization of the right colon, preliminary to its resection. It facilitates matters to mobilize at least six inches of the terminal ileum. Rankin, in his recent monograph, agrees with him. One opens the peritoneal cavity at the outer border of the right rectus. If necessary, this wound can be enlarged outward by a lateral separation of the lateral muscles. An incision through the right rectus does not permit the same facility to enlarge the wound, and one is apt to be bothered with the deep epigastric vessels. After orientating the mass and examining the mesentery for glands and deciding that it is operable, even if there is metastasis to the liver or to inaccessible lymph-glands, I believe the patient is made more comfortable for the time he has to live by resection than the side track anastomosis. In the first place, palpable lymph-glands do not mean involved glands. In the second place, it is difficult to palpate and impossible to see the liver from this low wound.

The cæcum, the appendix and the ileum are lifted up. The outer peritoneal fold of the mesentery of ileum and cæcum are divided with the knife and separated by blunt dissection as near as possible to the gut, but a good distance from the involved area. This peritoneum is nicked and separated along the ascending colon up to the point where the colon is to be divided. If

one plans resecting the entire colon, carry this mobilization up until the hepatic colon is mobilized. Then one lifts up the ileum and colon, finds and divides the vessels in the inner fold, again saving as much peritoneum as possible. This is done in order to cover the raw surface left by the removal of the large gut. If there are any palpable glands, remove them with as wide a margin as possible, or one can remove a gland with the cautery and make a frozen section. If the gland is involved, proceed to the limit of glandular removal; if it is not involved, do not sacrifice so much peritoneum of the mesentery.

The question is as to how to ligate the vessels. My experience urges clamping the vessels, dividing between the clamps and ligating, either with fine silk or 00 chromic catgut. In experiment on dogs one can ligate these vessels with a straight intestinal needle, threaded with fine silk, and have no difficulty, but on the human being it requires more tension on the ligature to stop bleeding than the method of clamping first. It is difficult to prove, but my impression is that there have been fewer cases of embolism from the ligated mesenteric vessels and even the omental vessels if they are clamped and tied rather than ligated without clamping. Also, the ligature is less apt to slip than when tied over a clamp.

There is really nothing difficult in the resection of the entire right colon. It takes a little more time if it is carried to the mid-colic artery in the transverse colon, but there should be no more mortality. I began with my first case in 1911 (Fig. 16) by making a complete resection to the middle colic artery. Since then, except on few occasions, I have resected distal to the tumor, selecting a good vascular area, as shown in Fig. 16 at X. It makes no difference where you divide the colon, the most important thing is circulation. The next is proper inversion, as already described. It seems to make little difference how you anastomose the ileum to the colon. I have never selected end-to-end. I have usually chosen lateral with the two ends pointing out and have frequently brought these two ends out, as shown in Fig. 19. But when the rent in the right peritoneum cannot be sutured, instead of leaving a huge raw surface there I have risked the leakage from the inverted end of the colon and sutured the colon into the rent. But when this is done I always suture the ileum over the inverted end of the colon. So far, fortunately, there has been no leakage. It is interesting to note that I have learned very little in the technic of the resection of the right colon since the experience of my first case in 1911, and at this time I was greatly helped by Mayo's article and Halsted's experimental work on dogs in preserving the circulation of the divided end of the gut.

Apparently Inoperable Cancer of the Right Colon.—In one instance, an operator of experience explored because of a palpable tumor in the right lower quadrant and decided that the condition was inoperable. In one (Ballouz, Path. No. 15,788) the operator (1914) anastomosed the ileum to the transverse colon. Later, by immobilization of the right colon, I could demonstrate that it was adhesions and not new growth that impressed the

first operator that the colon could not be removed with the cancer, and the palpable glands were not metastatic. In this case it was necessary to remove the colon to the mid-colic vessels. I examined this patient a few days ago (1932). There are no signs of local recurrence or metastasis. He still now and then has slight attacks of diarrhœa. This is the objection to complete resection of the right colon for cancer unless it is essential to allow a more complete removal of the disease. The more of the right colon you remove from a patient with malignant disease, the greater is the risk of an annoying post-operative diarrhœa.

It is remarkable that when you resect the same amount of right colon for ptosis, as advocated by Lane, of London, you do not observe this diarrhœa.

Chronic Inflammatory Tumor of the Cæcum.—Doctor Sowers, Resident Surgeon of the Johns Hopkins Hospital, explored a tumor of the cæcum in 1905, decided it was inoperable, removed no tissue for microscopical diagnosis. This patient was traced for nineteen years and we then were informed that she died of other causes. Such observations are of great importance when we estimate the cures of real cancer. Had this patient been treated after she left Johns Hopkins Hospital by some cancer cure the public could have been informed that the diagnosis of inoperable cancer had been made after an exploratory operation in that hospital.

When the tumor is situated in the hepatic flexure or right colon and its proper resection would force an end-to-end anastomosis, it is my opinion that the safer procedure would be a complete removal of the right colon with the safer suture of ileocolostomy. If, however, one can resect and suture by the lateral method, or my method, it might be wise in some instances to choose this way. I am confident that my patient operated on some weeks ago for a cancer in a very redundant right colon in which I chose local resection and lateral anastomosis by my method, would have run no more risk and saved much time and money had I performed a complete resection of the right colon.

Cancer of the Mid- or Transverse Colon.—The personal experience of any single surgeon is limited. Doctor Raiford found, as I know, and as most experienced operators know, that the mortality after resection of the transverse colon with any form of anastomosis other than the method described here by me has had a too high mortality. Part of this may be explained by improper pre-operative preparation, that is, failure to have a clean colon. Perhaps some of the mortality could have been eliminated by a pre-operative appendicostomy, which I am now employing with few exceptions in every case of resection of the colon itself in which the cæcum is not removed. It is an operation that can be done under novocaine. It relieves obstruction if it is present. It also shortens the time of pre-operative preparation. In my own case of end-to-end anastomosis of the transverse colon I placed the suture extra-peritoneally by putting the omentum behind it and suturing the gut on each side of the suture line to the peritoneum of the abdominal wall. This patient recovered in spite of a slight leakage. I had no choice in this instance. I have mentioned the case before. The patient was acutely ill following the

drainage of the gall-bladder. The transverse colon seemed too short even to allow a Mikulicz. I could give the palpable disease but a very narrow margin, and the suture had to be done under some tension.

It was the study of the pathology in this case and the ultimate good result that first impressed me that operators gave malignant disease of the colon too wide a margin. This is unnecessary. The place to give a good margin is the mesentery with the glands. In both stomach and colon the advice to give wider margins is based upon pathological studies of practically hopeless cases and is not confirmed by recent pathological studies in my laboratory. Doctor Raiford is now at work on the confirmation of this statement. So far, he has found nothing to indicate that this statement is not correct.

Cancer of the Splenic Colon.—The difficulty here is the mobilization of the colon. It can't be done in the usual way without too big a wound. In my few cases I have ligated the vessels first and then gone through and divided the peritoneum on the other side. Many of these cases become inoperable quickly on account of adhesions. A few come under observation with acute obstruction. One, I remember especially, of a colleague of mine, who, operating for acute obstruction, found the descending and sigmoid colon collapsed and the left transverse dilated. With the hand he could feel up to the splenic flexure a small tumor with a ring-like contraction. Looking upon it as benign, he anastomosed the left transverse with the sigmoid colon. Four and a half years later the patient, up to this time free from all symptoms, developed the signs of an abscess in the splenic area. When I explored it, it was a broken-down carcinoma due to the invasion of the original cancer in the splenic colon.

Cancer of the Descending Colon.—This is a rare situation almost as difficult to mobilize as the splenic colon and more difficult to suture. I have not had sufficient experience to justify any advice as to methods. I would recommend appendicostomy whether there is obstruction or not. I would mobilize the bowel in the position of the cancer above and below and if possible bring out the colon with the tumor after the method of Mukulicz and then employ my suture. If this could not be done, and I was not certain of my end-to-end anastomosis, or if there was too much tension for end-to-end anastomosis, I would bring the two ends out at separate places in the wound, suturing a tube in the upper and closing the lower. If the patient was not in good shape, I would postpone an anastomosis between the sigmoid and the transverse colon. I trust that Doctor Raiford's paper will ascertain the cause of the large mortality after resection of cancer in the mid, transverse, splenic and descending colon.

Cancer of the Sigmoid Colon.—This is one of the most common situations, and if the sigmoid is redundant there should be no difficulty in mobilization and proper resection. The difficult question to decide is the method of suture, when there is a choice other than end-to-end. There is no question that the method of Mikulicz in bringing the tumor out and making the lateral suture with two ends out recommended here, has the least mortality. Yet Halsted,

in 1902, in his first operable case of sigmoid cancer, made a successful end-to-end suture after resection. The patient lived in comfort six years. I had a similar successful resection and end-to-end suture in 1906. Almost every operator of experience has had similar success. But I am not convinced that end-to-end suture is safest here or should be the suture of choice rather than the suture of necessity. I would also recommend, as already mentioned in this paper, preliminary appendicostomy.

Sigmoiditis and Diverticulitis.—Not infrequently these two benign lesions of the sigmoid colon may give rise to identical symptoms. Even the study of the fluoroscopical picture and X-ray film may simulate cancer. When the abdomen is explored, whether there is obstruction or not the mass to be palpated may feel and look like cancer. These non-malignant inflammatory lesions will even suggest inoperable cancer and it is fortunate for the patients when they are apparently inoperable because they recover from the colostomy and live for many years, long enough to exclude cancer, and in the majority of instances the colostomy closed spontaneously or can be closed. If the patient is very stout and a bad operative risk and the lesion of the sigmoid difficult to remove, it is wiser to do a high temporary colostomy first. At the second exploratory laparotomy the inflammatory lesion may show such changes of improvement that its benign character can be recognized. My records show that in recent years the majority of these inflammatory lesions have been recognized and at least resection has not been performed on very difficult cases with fatal results.

Cancer of the Rectosigmoid Colon.—To accomplish a successful resection, with or without restoration of the continuity of the bowel, has been a difficult problem and still is. Even Kraske, in 1885, gives considerable space in his article to the difficulty of removing through the sacral route cancer in this region. In Surgery, Gynecology and Obstetrics, for August, 1906, I reported my first successful case of resection of a cancer in the rectosigmoid area by the so-called combined abdominal and sacral route. In addition, I was able to restore the continuity of the bowel by a suture of the end of the mobilized sigmoid brought down the abdominal cavity to the remaining half of the lower rectum, which had been undisturbed in the resection. This patient was ideal for this type of operation, very thin and wiry, and a good operative risk. I have already mentioned that this case, some nine years later, recovered from a resection of a similar cancer in the right colon, and then died a few months later of nephritis. In 1920, I fortunately had a similar successful case. This patient was also a good operative risk and had a redundant sigmoid. This patient is well in 1932 and until very recently was a railroad engineer.

In spite of these two fortunate experiences, I have not tried this operation in the last ten years, and I gather from the literature and the experience of my colleagues that a very few if any are taking this added risk of restoring the continuity of the bowel.

Tumors in the rectosigmoid area should first be explored, and I prefer

preliminary appendicostomy under novocaine. At the second operation, one must decide if it can be done from above alone. There are two methods: Divide the peritoneum around the rectosigmoid and isolate the gut and if possible divide, suture and invert the gut below the tumor. Then remove the colon with its mesentery and glands until you reach the proper position above the growth. Then divide the sigmoid colon again, remove the colon, and make a colostomy.

When this cannot be done, we have a choice between the combined removal by abdominal and sacral route of the mass in the rectosigmoid, or the division of the sigmoid colon above the mass and the isolation of the mass below and the suture of the peritoneum above it, and the making of a colostomy of the upper sigmoid loop (method of Robert C. Coffey, of Portland, Oregon). My personal experience so far leads me to prefer the Coffey method in cases of this kind. My first case, which was eminently successful nine years ago, is living today.

The Method of Miles, of the Cancer Hospital, London.—In the hands of this dexterous and widely experienced surgeon, the mortality has been extremely low. Personally, I cannot accept his method for my cases. Remember, Miles, by the combined abdominal and sacral route, removes the rectum from anus to sigmoid irrespective of the situation of the tumor, without preliminary colostomy and without removal of coccyx or sacrum. A number of operators in this country follow the Miles technic and reduce the danger of shock by blood transfusion. One must remember that whether you use Miles technic or Coffey's or any other modification, there must be a colostomy, and the ultimate comfort of the patient rests upon the colostomy.

When I am able to remove the rectosigmoid cancer from above, I leave the lower bowel alone. When I must do a combined resection for a high cancer of the rectum I leave the anus and uninvolved rectum alone. At present I am against the combined abdominal sacral operation in one sitting and prefer the Coffey. I still think it is safer if the cancer of the lower rectum can be removed successfully from below in one sitting, even if the peritoneal cavity must be opened, to adopt this method. The patient can have an abdominal colostomy if the lower one is not suitable.

Colostomy.—At present I would recommend first appendicostomy, which is kept open as a permanent functioning opening into the cæcum; second, when the colostomy is made to close the end of the colon, invert it, suture it into the abdominal wound laterally, and if there is a working appendicostomy do not open it until you are forced to, until the wound is healed. Then make a small opening. The patient can control everything except gas now and then. All patients wash the colon through the appendicostomy. One of my patients irrigates only twice a week and is perhaps the most comfortable of all.

Conservative Operations for Cancer of the Lower Rectum and in the Region of the Anus.—I will mention two cases, one of which will be illustrated (Figs. 4, 5, 6, and 7). The first was referred to me by my colleague,

Dr. William S. Thayer. The symptom of blood in the stools had been present but a few weeks. The proctoscope revealed a small polypoid tumor on the side toward the coccyx. The operation consisted of the removal of the coccyx, the opening and inspection of the upper rectum, the removal with a sufficient margin of the visible palpable tumor about the size of the end of the thumb, the complete suture of the rent in the rectum, and the partial closure of the external wound. This patient, of course, had complete control. The microscopical study shows a beginning cancer in the base of a polypoid tumor. In the future there will be more and more of such cases. Many will be found in periodic examinations if the proctoscope is used. In the second case, the mass was the size of the end of the thumb. It was situated in the anus, over the sphincter. It was a recurrent tumor, after an incomplete removal of a polypoid tumor microscopically malignant, and the growth was not checked by post-operative irradiation with X-ray. Under rectal anæsthesia, we removed with the cautery a piece of the recurrent tumor, demonstrated microscopical malignancy. Then, with the cautery, we removed the tumor with a good margin, just as we remove a lesion of the lower lip, a v-shaped mass of mucous membrane and skin with a portion of the sphincter muscle. The margins were then submitted to frozen sections, and as we had microscopical evidence that the recurrent local disease had been excised with sufficient margin, the wound was closed, catching the divided sphincter muscle in the suture. The remarkable result in this case is the good function. Unless he has a diarrhœa from indiscretions in diet he has perfect control, providing he empties his colon and rectum with enema in the morning.

Before writing these pages I had before me every history of cancer of the colon and rectum recorded in the Surgical Pathological Laboratory of the Johns Hopkins Hospital since 1889. I read in detail the histories of most of my personal cases. In these records there is a detailed description of every operation. I glanced over many of the early histories. Doctor Raiford went over with me his tables and we discussed his conclusions, mortality figures, and final results. So these pages are not written from memory only, but every definite statement is carefully checked from the original data. It was the first time that I had ever read Kraske's article, written in 1885. I learned the Kraske operation from Halsted and got my chief points on the resection of the right colon from William J. Mayo.

I hope the following somewhat new presentation of selected cases with illustrations will be helpful to those operators whose experience at this time is limited.

Preliminary Pre-operative Irradiation.—When the cancer involves the anus and its removal means a complete resection, even a complete Kraske, and the patient is old and a bad operative risk, no harm is done by at least trying pre-operative irradiation, especially if large amounts of radium are available and a very experienced and competent radiotherapeutist. At the present writing my experience is too small to justify more than this statement.

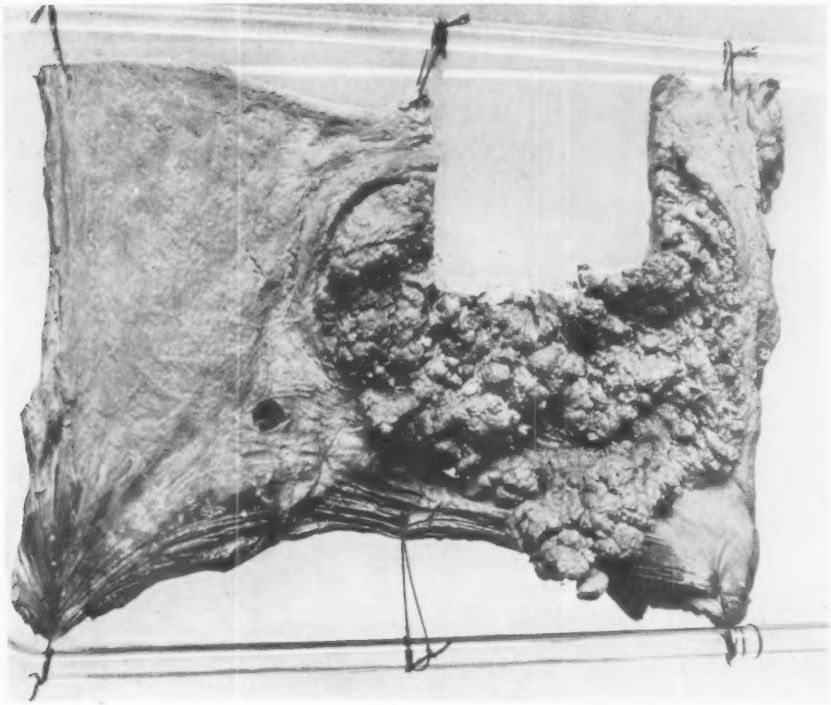

FIG. 1. (Path. No. 3193.)—Photograph of resection of the lower rectum with anus in 1900, by Kraske method. Peritoneal cavity not opened. Lived twenty-nine years. Glands not involved. (See Figs. 2 and 3 for microscopical pathology.)

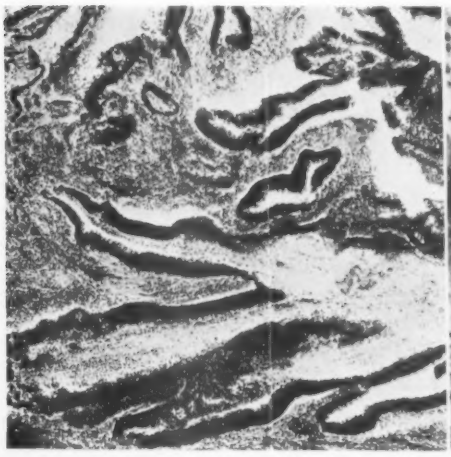

FIG. 2.

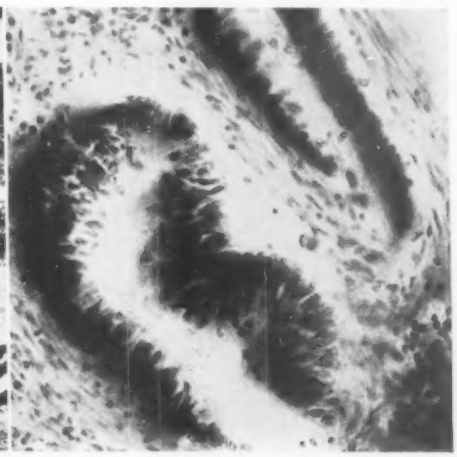

FIG. 3.

FIG. 2. (Path. No. 3193.)—Low-power ulcer shown in Fig. 1. This has been diagnosed adeno-carcinoma. Cells of a glandular type. Suggestive of low malignancy. Patient lived twenty-nine years.

FIG. 3.—High-power of tumor shown in Fig. 1. Adenomatous arrangement preserved. Cells glandular type but of the morphology of the malignant cancer-cell. Metastasis is frequently observed in adeno-carcinoma of the rectum and colon of this type. Practically all the cured cases are of the adeno-carcinomatous arrangement, with cancer-cells of this low-grade glandular type.

CASES OF CANCER OF THE RECTUM.—Figs. 1, 2 and 3. (Path. No. 3193.) Date of operation, July, 1900. Patient died, 1929, aged ninety years, twenty-nine years after operation, without any signs of local recurrence or metastasis. Fig. 1 is a photograph of the specimen removed after complete resection of the lower rectum following the technic of Kraske. The rectum has been split and shows the surface of the superficial ulcer.

Fig. 2 is a low-power and Fig. 3 a high-power photomicrograph, illustrating a low-grade adeno-carcinoma. The patient was a white female aged sixty-one years. She was a very intelligent woman, the wife of a clergyman; had observed some pain and bleeding for eight months after stool; consulted her physician, the late Doctor Scott, of Hagerstown, ten days before her admission to the hospital. Doctor Scott immediately made a rectal examination, felt and diagnosed the local condition, and made arrangements at once for her admission to the Johns Hopkins Hospital.

My note at that time in the hospital is as follows: "Per rectum the finger feels a superficial fungus growth to the right and anterior, beginning five millimetres within the anus. The finger could not get above the growth, but when the patient was under anæsthesia and the sphincter dilated we introduced Halsted's rectal speculum and could see normal mucous membrane above the growth.

At that time, 1900, Halsted and his associates had had considerable experience with the resection of the rectum after the method of Kraske. We had all learned from assisting Halsted how to do it. The patient was placed on the back and the pelvis elevated on a specially constructed block with leg pegs—a position now used for perineal prostatectomy, a position then used for the Whitehead operation for hemorrhoids. Halsted's speculum was introduced, the rectum inspected and cleansed, packed with gauze to which silk ligatures were attached. The anus was not sutured. A straight incision was made from anus to the middle of the sacrum. The coccyx and lower fourth of the sacrum were removed. Largely by blunt dissection, everything was cleaned out in the space between the rectum and sacrum. Then the anus and a zone of skin were encircled with a skin incision, the skin flap dissected back, and the entire rectum isolated as one mass with all its surrounding tissue to a position well above the growth, as shown in Fig. 1. When the patient was a male a sound was introduced into the bladder to protect the urethra. Rarely did we have any difficulty with the prostate. In a few instances, the prostate was partially removed, in one completely removed. Now and then one or both seminal vesicles were removed. None of these patients was permanently cured. As in the case shown in Fig. 1, the low position of the growth allowed its removal without entering the peritoneal cavity. In many instances, the peritoneal cavity is opened in order, not only to give the growth some margin, but to mobilize the sigmoid downward in order to make a proper sacral anus. In recent years when the new growth is situated high we prefer to make first a permanent sigmoid colostomy and appendicostomy and then resect the tumor and rectum from below with or without opening the peritoneal cavity and leave the upper portion of the colon. In some instances the lower rectum and anus, if not involved, remains undisturbed. I have just heard from a patient [and his physician] upon whom this method was employed. This method, when it can be done, is less dangerous than the plan of Coffey or the complete resection chiefly advocated by Miles, of London. When properly selected, one runs no more risk of local recurrence and just as large probabilities of a permanent cure. I am confident the mortality would be less than the more complete operations except in the hands of the most expert and experienced operators.

The wound left by the Kraske resection, whether combined with the abdominal route or not, takes time in healing. The convalescence is uncomfortable, even when there is an abdominal colostomy. There appears to be no other way of properly removing cancer of the rectum or rectosigmoid

colon. The removal of a piece of sacrum should be avoided if possible in order to relieve the patient of post-operative temporary catheterization of the bladder, not necessarily dangerous, but unpleasant.

Doctor Raiford confirms my observation up to date in the fact that there has been but one case with microscopically involved glands in the pelvis that has been permanently cured more than five years. In this case it is more than fifteen years since the operation.

From my experience the principles of the Kraske operation should remain unchanged today when indicated by the extent or position of the growth. They are as fundamental and fixed as Billroth's resection of the stomach and Halsted's complete operation for cancer of the breast.

Figs. 4, 5, 6, and 7 (Path. No. 41,354), illustrate the gross and microscopical picture of a polypoid tumor removed through the sacral route from the middle third of the rectum. The wound was closed, healed, and the patient had perfect function and is well three years since operation. The patient was referred by Doctors Thayer, of Baltimore, and Sloan, of Parkersburg, West Virginia, in February, 1929. The patient was a white female, aged forty-two years. A polypoid tumor the size of the end of the thumb (twenty-five-cent piece) could be felt with the index finger ten centimetres above the anus and clearly inspected with the proctoscope. It was sessile and not pedunculated. All examinations and laboratory studies were negative. The patient, though married, had no children. The probabilities are, had she had children and been subjected to the new rule to examine the rectum with the proctoscope when a pelvic examination is made, here would probably have been revealed the polypoid tumor when it was small and it could have safely been removed through the rectum with a snare. Seven years ago, when she was operated on for hemorrhoids, no proctoscopical examination was made. The patient had observed bleeding from the rectum for a year. During this year she saw a number of physicians because of her bleeding and gas pains, but received treatment without examination. Doctor Sloan, when consulted, demonstrated the presence of this polypoid growth at once, and referred the patient to Doctor Thayer.

Operation on the Tumor Shown in Figs. 4 and 5.—On account of its high position, we followed the basic principles of Kraske and removed the coccyx and a small piece of sacrum. This allowed us to open the rectum above the tumor. First, however, we removed tissue between the rectum and coccyx, made frozen sections, and found no lymphoid tissue and no cancer. The rectum was then opened by a longitudinal incision and we could see and feel the tumor, as shown in Fig. 4. There was no infiltration in the wall of the gut around its base. It was the size of a silver dollar, that is, larger than it felt per rectum with the finger or appeared in the proctoscope. The base of the tumor was one-half the diameter of its surface. The gross section of the tumor is shown in Fig. 5. There is no naked-eye evidence of any infiltration into the tissue removed beneath the base of the pedicle. This tissue consisted of the thin submucous wall of the gut and fat and fibrous tissue beyond. The immediate frozen sections were even clearer than the photomicrographs of the permanent sections shown in Figs. 6 and 7. Shall we call this a benign polypoid growth or carcinoma? Compare Figs. 6 and 7 with Figs. 2 and 3. They appear identical. The tumor in the gross from which the sections in Figs. 2 and 3 were taken was malignant. The gross appearance of this polypoid tumor of Fig. 5 suggests malignancy. From my studies of the benign type of adeno-carcinoma of the colon and rectum I am inclined to view all polypoid tumors as malignant or potentially malignant. The polypoid tumor with a sessile base should be removed by resection or at least the complete wall of the gut beneath and around the base.

We have two cases of lesions diagnosed polypoid tumor in the rectosigmoid colon. Both were removed from below through the proctoscope by a snare. Both recurred.

And later I removed them by resection of the sigmoid colon through the abdominal route with end-to-end suture. The recurrent tumors were microscopically malignant.

FIG. 4.

FIG. 5.

FIG. 4. (Path. No. 41,354.)—Polypoid tumor mid-third of rectum removed with zone of normal mucous membrane through sacral wound. Photograph of surface showing the raised, somewhat fungated cauliflower sessile polypoid mass, stained with hæmorrhage. (See Fig. 5 for section.)

FIG. 5. (Path. No. 41,354.)—Cross-section of tumor shown in Fig. 4. The surface suggests cancer rather than benign polypoid tumor. It is circumscribed at the base and removed with a margin of an uninvolved gut and fat.

The patients, however, still remained well three and five years after the operation. When you grasp a polypoid tumor and lift it and demonstrate that it has a pedicle of normal

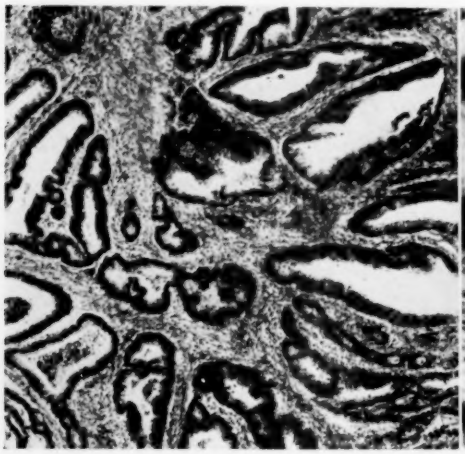

FIG. 6.

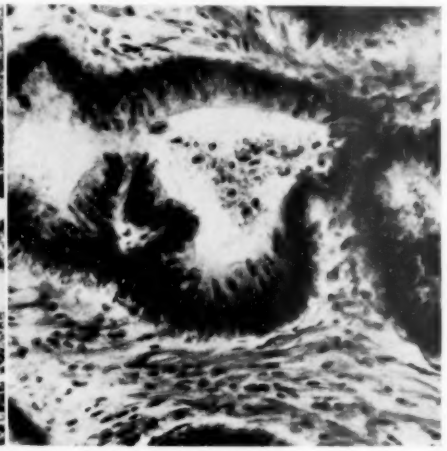

FIG. 7

FIG. 6.—Low-power photomicrograph of tumor in Fig. 5. Is this a benign in a polypoid growth or an adeno-carcinoma? Compare with Fig. 2.

FIG. 7.—High-power photomicrograph of tumor shown in Fig. 5. Compare with Fig. 3, a typical gross cancer of the rectum.

mucous membrane, you can remove it locally, which I have done recently on a few occasions.

Closure of Wound in Case Shown in Figs. 4 and 5.—The opening into the rectum was closed with interrupted ⁰⁰ chromicized catgut with here and there a continuous suture. The second layer was continuous catgut reinforced with fine silk. The external wound in the skin was partially closed above and below. The wound healed without leakage of gas or fecal matter, and within two weeks the external wound was healed. It is now almost three years since the operation. There is perfect function and no return of symptoms.

Cancer of Rectosigmoid Colon.—Removed by combined abdominal and sacral route with restoration to normal by end-to-end suture in the sacral wound.

Fig. 8. (Path. No. 6550.) This illustration taken from a sketch is republished from Fig. 3, Surgery, Gynecology, and Obstetrics, August, 1906. The lower third of the sigmoid and the upper third of the rectum have been removed with the cancerous tumor by the combined route. The upper sigmoid has been mobilized and drawn into the sacral wound. The peritoneum has been sutured to the sigmoid, closing off the peritoneal cavity. The mobilized sigmoid has been sutured to the lower third of the rectum in the sacral wound. There is a temporary lateral colostomy above. This operation was performed by me at Johns Hopkins Hospital in 1905. A small fistula developed at the site of the end-to-end suture in the sacral wound. There was ultimate healing with a small sinus. This gave the patient some trouble from time to time. I have alluded to this case in the text. Eight years later, in 1913, the right colon was resected for a second carcinoma, and the patient died a few months later of nephritis. This diagram in Fig. 8 illustrates the different possible types of the combined operation. I. the most radical, the entire rectum and colon are removed and the lower end of the upper sigmoid remains as a permanent colostomy in the abdominal wall. In the Coffey the same colostomy remains. The first operation is entirely abdominal. A portion of the sigmoid colon, closed and inverted above the cancer of the lower sigmoid and upper rectum, is pushed beneath the rent in the pelvic peritoneum and then the rent is sutured. This places the malignant disease with the surrounding and lower gut extraperitoneal, to be removed later through the sacral wound. Coffey writes me he still drains by an incision in the sacral area to this subperitoneal space in which the inverted end of the depressed gut is situated. I have never used the drainage, which seems unnecessary if you properly close, invaginate and suture the colon above the tumor. The majority of operators following the Coffey technic at the second operation through a sacral wound remove the entire gut, including the anus. In recent years I have restricted the resection to the upper portion, leaving the anus and lower third of the rectum. It seems to be a simpler procedure and leaves a smaller wound to heal by granulation. We must remember, however, the possibilities of secondary polypoid growths in the gut left behind. If it is possible to divide the gut below the growth through the abdomen, with or without dividing the peritoneum around the gut in the depth of the pelvis, then one lifts the tumor and upper gut out of the peritoneal cavity and performs a permanent colostomy of the end of the colon left behind. The lower gut is closed and invaginated and placed extraperitoneally just as in the Coffey operation, but the lower rectum is left intact, as the tumor has been removed through the abdominal wound. These are the various possible combinations. Doctor Raiford is attempting from a study of our own cases and the literature to estimate the mortality of the different methods, but there are many factors in operative mortality that have more to do with the condition and vital resistance of the individual patient than with the technic of the operation and skill of the operator. There is no question that we should choose the operation of least risk in the resection of cancer of the rectosigmoid colon. In the first place, there is a choice. A more extensive removal above and below the tumor area with a more extensive removal of the mesenteric area or tissue in the sigmoid extraperitoneal space is unnecessary to give the patient a better chance of a permanent cure. The operable malignant area of the colon does not require a wide margin of uninvolved gut, and as metastasis to glands practically makes the case

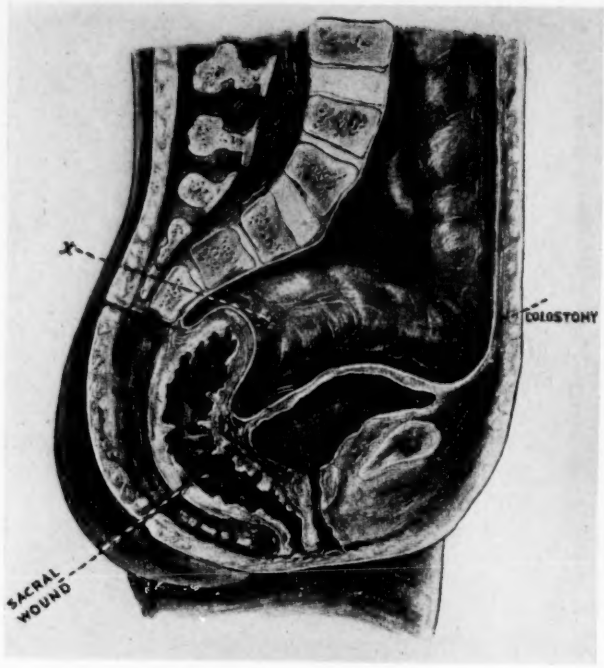

FIG. 8.

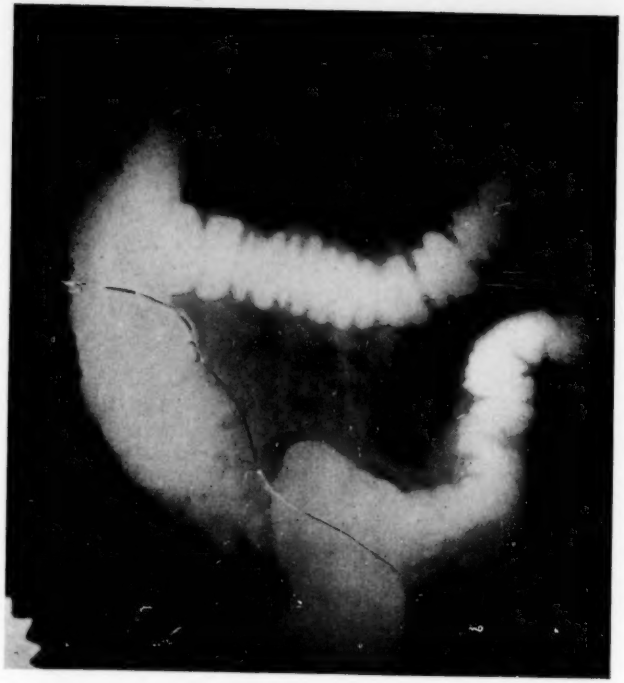

FIG. 9.

FIG. 8. (Path. No. 6550.)—From Fig. 3, Case 1, Surgery, Gynecology and Obstetrics, August, 1906. Diagram illustrating relation of parts after the complete combined operation for cancer in the rectosigmoid colon and end-to-end suture of colon to lower rectum in the sacral wound. X—suture of peritoneum around colon in floor of pelvis. Opposite sacral wound end-to-end suture. Opposite colostomy, lateral temporary abdominal colostomy.

FIG. 9. (Path. No. 24,433.)—X-ray after bismuth per rectum. Three years after operation of a case similar to that shown in Fig. 8. The operation in the case shown in Fig. 9 was practically identical to that illustrated in Fig. 8. In both there was a slight leakage at the site of the suture. In both the temporary colostomy closed spontaneously and function was restored. The patient illustrated in Fig. 9 is living today, almost twelve years after operation. He was able to continue his duties as a railroad engineer and sent me a photograph of himself and his engine five years after his operation.

hopeless, it is unnecessary to risk post-operative death in order to remove more of the glandular area. My recent experience teaches me to perform under local anæsthesia appendicostomy first except where the cancer is in the anus and in the low rectum so situated that it can be completely removed by a low resection. If the patient does not prefer the sacral anus a permanent colostomy can be performed later. When there is an appendicostomy the next stage is a laparotomy. If the tumor cannot be completely removed from above I prefer the Coffey operation in two stages. In thin people it is less difficult to operate from above alone. In more deeply situated tumors the peritoneum can be divided and the tumor isolated below, the gut divided between clamps with the cautery, the lower gut closed, even without a peritoneal surface, with three rows of fine black silk. A rectal tube can be passed per rectum, as Coffey does, to aid in more thorough invagination. Then the peritoneum can be closed over this lower portion. There is no doubt that the difficult part of the operation is in the lower pelvis of the abdominal cavity, but the operation with the greatest element of shock is the sacral operation. If possible, the abdominal and sacral, if they must be done, should be done in stages. Appendicostomy with proper pre-operative preparation and blood transfusion is reducing mortality from shock. The danger of end-to-end suture deep in the pelvis, with or without a tube, or by Halsted's buttress suture, is so difficult even in the hands of the experienced operator and the danger of peritonitis from faulty circulation of the ends of the gut so great that I prefer a permanent colostomy to this attempt, although I have had a number of successful cases.

Fig. 9. (Path. No. 24,433.) An X-ray after bismuth per rectum, three years after an operation similar to that shown in Fig. 8. The operation in the case shown in Fig. 9 was practically identical to that illustrated in Fig. 8. In both there was a slight leakage at the site of the suture. In both the temporary colostomy closed spontaneously and function was restored. The patient illustrated in Fig. 9 is living today, almost twelve years after operation. He was able to continue his duties as a railroad engineer and sent me a photograph of himself and his engine five years after his operation.

This paper cannot be lengthened any more by discussion of the details of the various methods of preparation for and operative attacks on cancer of the colon situated too deep in the pelvis for safe resection and suture, or so situated that resection and suture are impossible or must be done in the sacral wound. I have read over a series of operative notes dictated by me during or directly after the operation and at this time I feel it inappropriate to put them into the literature. Perhaps it would be helpful to my own associates and interne staff in the hospital to read them over after assisting at such an operation, but they are appropriate only for a very large monograph or book. I hope ultimately they will be as helpful as Kraske's description of his technic in 1885 and the Mayo Brothers' contributions to the surgical technic of resection of the colon from cæcum to anus.

Resection by Coffey's Method.—Figs. 10, 11, and 12. (Path. No. 35,822.) Pictures of the gross and microscopical pathology of a tumor situated in the upper rectum which was removed by a modified Coffey operation in 1924. The patient is well today, almost eight years since operation. The microscopic pathology in Figs. 11 and 12 should be compared to Figs. 2, 3, 6, and 7. This case still retains the picture of an adeno-carcinoma. The cells, however, appear more malignant. The glands were not involved. At the time of this operation in October, 1924, I found that I could feel the mass per rectum. You will observe in Fig. 10 the anus to the right and the tumor to the left. It seems so small and so accessible from below with apparently sufficient margin of rectum below it that I planned to resect it and restore the continuity of the bowel by suture in

the sacral wound. The patient was very averse to an abdominal colostomy, and up to that time I had not succeeded in giving perfect control. I performed appendicostomy first,

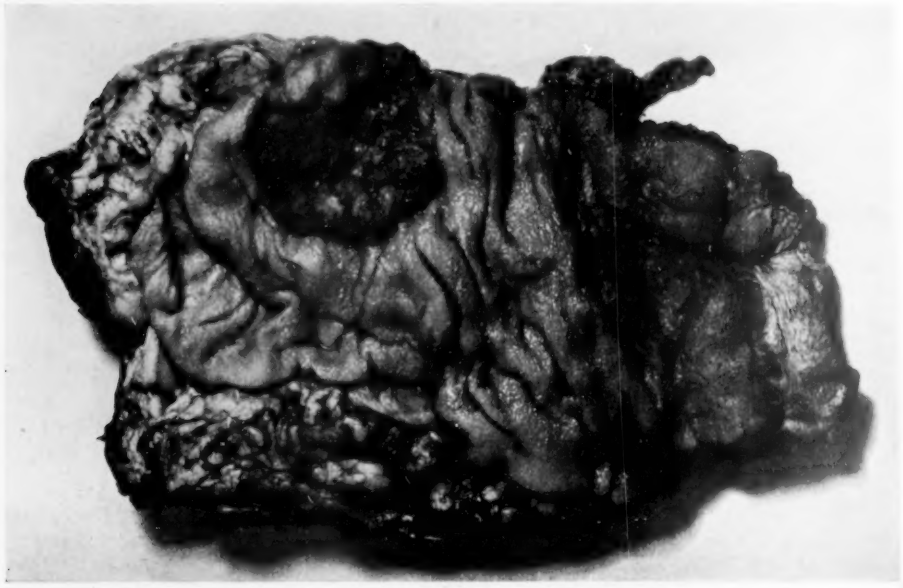

FIG. 10. (Path. No. 35,822.)—Photograph of the resected lower half of the rectum through the sacral wound, in the second stage of the Coffey operation. In spite of the small operable ulcer which could be easily felt with the index finger in the rectum there had been pain and bleeding for a year. No recurrence to date, almost eight years. (See Figs. 11 and 12 for microscopical picture.)

because the patient was not a good risk and I felt in this way I could give him better pre-operative preparation. I then explored and could not palpate the tumor above. As

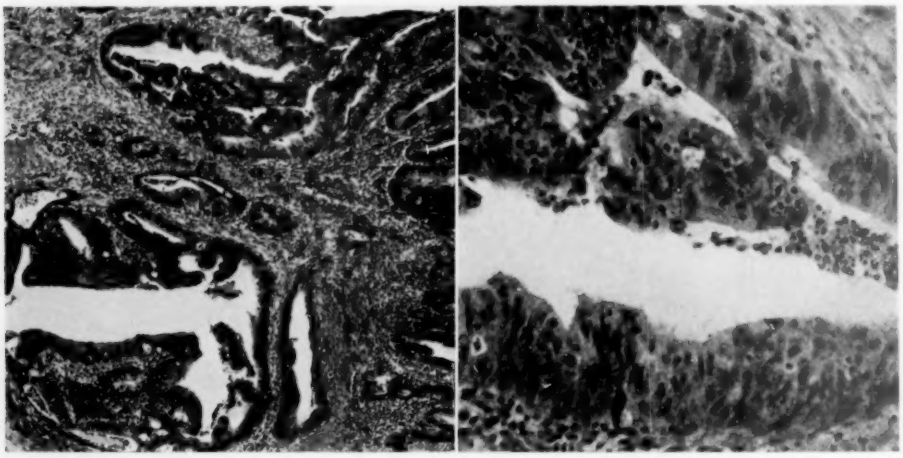

FIG. 11. FIG. 12.

FIG. 11. (Path. No. 35,822.)—Low-power ulcer rectum, shown in Fig. 10, diagnosed adeno-carcinoma. Glands not involved. Well, no recurrence, almost eight years.

FIG. 12. (Path. No. 35,822.)—Section shown in Fig. 11. Morphologically, glandular cells are malignant and suggest a higher grade of malignancy than those in Figs. 7 or 3.

the patient was not in good shape I changed my mind to the first stage of the Coffey operation. In making the permanent colostomy I closed and invaginated the end of the

colon and sutured it laterally in the upper portion of the abdominal wound. It had to be done hurriedly as the patient was showing signs of shock. On account of his condition I was not able to make as painstaking an invagination and suture of the gut above the growth in the lower pelvis. However, I made a thorough suture of the rent in the peritoneum and sutured the bladder over it as a further safeguard. Ten days after operation, on account of fever and leucocytosis, I removed a portion of the coccyx and sacrum and extirpated the tumor and the rectum through the sacral wound. There was an accumulation of blood-stained fluid in the cavity about the sutured end of the gut and cultures grew colon bacilli. This demonstrates the value of Coffey's drainage when your

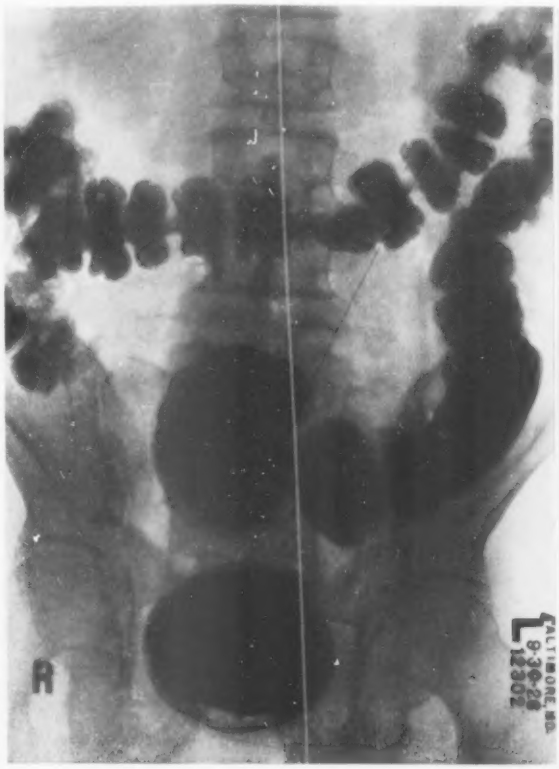

FIG. 13.

FIG. 14.

FIG. 13. (Path. No. 38,406).—This X-ray pictures a typical hour-glass filling defect in the lower sigmoid. In this case the tumor was situated sufficiently high to allow resection and end-to-end suture in the pelvis through the abdominal wound. For specimen removed see Fig. 14.

FIG. 14. (Path. No. 38,406.)—Photograph of specimen shown in X-ray (Fig. 13.) The narrow margin of gut below the tumor was due to a low position of the palpable mass in the pelvis. Nevertheless, it is sufficient margin for the malignant area. The longer portion of the gut above is explained by the redundant sigmoid. The end-to-end suture was successful. The morphology of the cancer-cell in the tumor in this case was very malignant, and in spite of the operability of the local growth the patient died of metastasis within four months.

technic is faulty. The patient had a long and tedious convalescence, because of the slow healing of the wound. However, he has been compensated with a perfect function of the appendicostomy and sigmoid colostomy. The appendicostomy admits the smallest catheter; the colostomy just admits the little finger. He has tried various methods of irrigation. The one that works best is an irrigation every two or three days with a catheter through the appendicostomy. He wears nothing but some gauze and an ordinary abdominal binder. There is no leakage of fecal matter. Now and then a little gas escapes, especially when he is playing cards at night. "Then," he says, "he blames

it on the other fellow." This case has demonstrated to me the great value of preliminary and permanent appendicostomy, and the proper method of making a colostomy which will not prolapse and not leak except now and then gas. Function here is far better than that usually obtained by a sacral colostomy, although the function in the case illustrated in the case Fig. 1 was ultimately as perfect.

Every attempt should be made to give these patients the best functioning colostomy. This can always be done at a secondary operation when the first resection is safer with a sacral anus.

Cancer. Resection Sigmoid—End-to-End Suture in Pelvis.—Figs. 13 and 14.

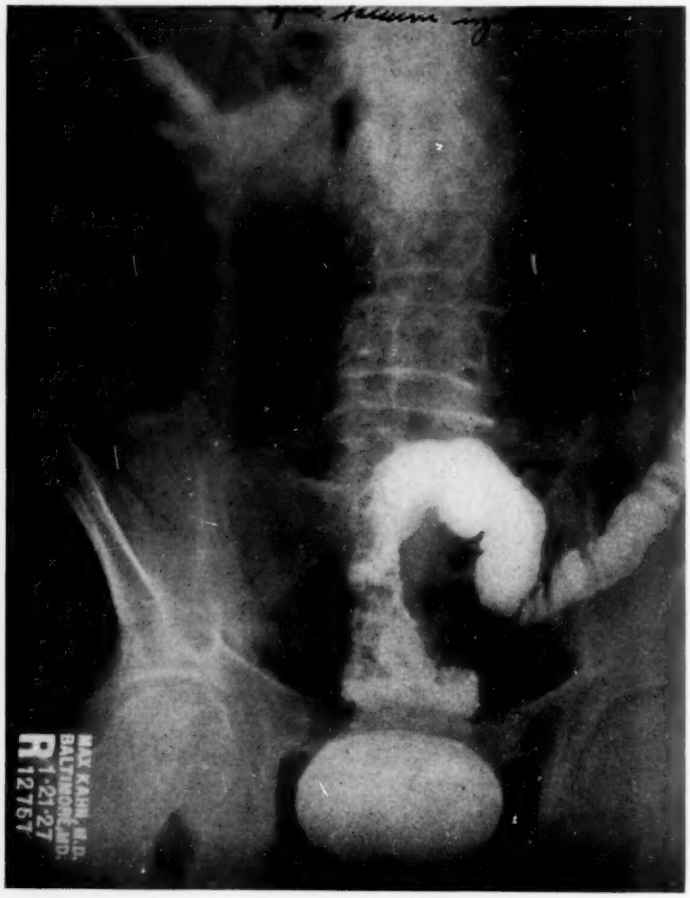

FIG. 15. (Path. No. 3887.)—X-ray of a cancer of the rectosigmoid with symptoms of three years' duration, and after X-ray treatment over a period of more than two years. (See text for details.)

(Path. No. 38,406.) Fig. 13 demonstrates how clearly some tumors of the colon give an hour-glass filling defect which allows an almost positive diagnosis of at least a lesion that should be subjected to exploratory operation. The photograph of the specimen removed is shown in Fig. 14. We were able to resect this palpable mass from above by giving it the narrow margin below shown in the photograph and perform a successful end-to-end anastomosis. That more gut was removed above the tumor was due to a very redundant sigmoid. Removal of this extra-long piece simplified end-to-end anastomosis and left ends of gut with better circulation. A temporary lateral colostomy was made

above the suture. No glands could be seen or felt. The patient returned after four months of comfort with signs of partial intestinal obstruction and much fluid in the peritoneal cavity. An exploratory laparotomy revealed fluid, glandular metastasis everywhere, but no obstruction at the point of anastomosis, but higher up in the small intestine, due to mesenteric-gland involvement.

The result in this case can first be explained by delay. This patient had definite symptoms for three and a half years, sufficient to justify a proctoscopical examination and the X-ray study after bismuth per rectum. Finally, obstructive symptoms of such a degree brought him under the observation of a physician who made an immediate complete examination and found the cause and site of the trouble. Second, the microscopical sections of the tumor shown in Fig. 14 show a high-grade, fully developed carcinoma, in great contrast to the microscopical pictures that we have reproduced in this article. Unfortunately, the photomicrograph of this case has been mislaid, and cannot be reproduced. You will observe in Fig. 14 the type of a cancer of the large gut that produces a small tumor area but marked annular constriction. This is not always associated with long symptoms or a morphologically more malignant type of cancer cell. We cannot explain why some tumors remain an ulcer without obstruction and may be very extensive and yet superficial and why other local growths constrict and others perforate, producing a general carcinomatosis of the abdominal cavity.

Fig. 13. (Path. No. 30,406.) This X-ray pictures a typical hour-glass filling defect in the lower sigmoid. In this case the tumor was situated sufficiently high to allow resection and end-to-end suture in the pelvis through the abdominal wound. For specimen removed, see Fig. 14.

Fig. 14. (Path. No. 38,406.) Photograph of specimen shown in X-ray. (Fig. 13.) The narrow margin of gut below the tumor was due to a low position of the palpable mass in the pelvis. Nevertheless, it is sufficient margin for the malignant area. The longer portion of the gut above is explained by the redundant sigmoid. The end-to-end suture was successful. The morphology of the cancer-cell in the tumor in this case was very malignant, and in spite of the operability of the local growth the patient died of metastasis within four months.

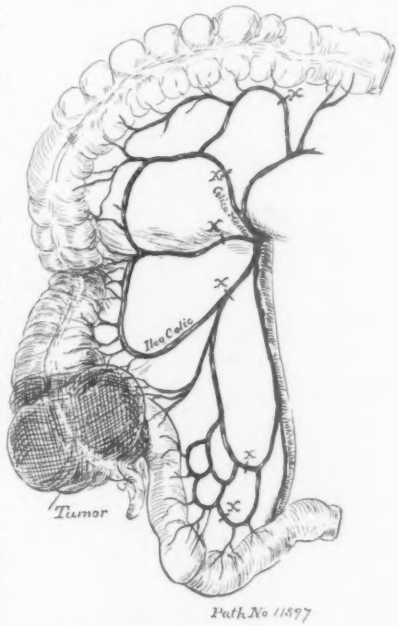

FIG. 16. (Path. No. 11,597.)—Diagram of anatomy of first portion of ileum and right colon, to illustrate operation, resection of right colon, 1911.

Cancer or Sigmoiditis.—Fig. 15. (Path. No. 38,872.) This X-ray showing the involvement of the rectosigmoid colon, which had not produced obstruction, was taken three years after symptoms and one year and six months before death from metastasis.

This patient came under my observation with a diagnosis of cancer of the upper third of the rectum, based upon a proctoscopical examination and X-ray. He had been given repeated deep X-ray treatment. He was fairly comfortable. When I explored the area I found it inoperable, because the bowel was adherent everywhere to the pelvis and lower lumbar vertebra. As the patient was comfortable and there was no obstruction, I decided to do an appendicostomy only, and again I could not tell whether the mass was cancer or sigmoiditis. If the mass was cancer, which it later proved to be, the X-ray had apparently produced a definite inflammatory exudate which we rarely ever see in cancer not treated in this region. This patient lived and worked in comfort for a year

and a half and then, on account of obstruction, was given the benefit of a sigmoid colostomy without investigation of the pelvic growth. The patient lived about a month after this operation. I have no way of determining the value of the X-ray treatment in this case. He was given deep X-ray without exploration and it was associated with a number of years of comfort. I also have no way of determining whether my appendicostomy put off the later colostomy. The X-ray treatment stopped the bleeding. I am inclined to the opinion that this patient should have been explored when his first bleeding took place, in 1924, more than four years before his death.

Cancer of Cæcum and Colon.—Fig. 16. (Path. No. 11,597.) This diagram was made in May, 1911, almost twenty-one years ago. It is a copy from an anatomy. I have already discussed it. It is to illustrate the point of the necessity of the operator to appreciate the circulation of the large gut as directing him where he shall make his resection, no matter what type of suture may follow. The circulation of the small intestine has much more collaterals and the danger of necrosis at the point of division is very slight as compared with the large intestine.

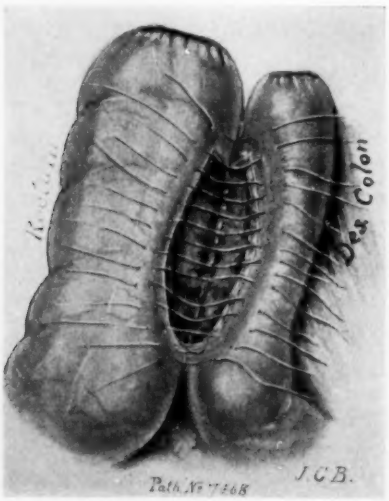

FIG. 17A.

FIG. 18B.

FIGS. 17 and 18.—From Fig. 6, A and B, ANNALS OF SURGERY, volume lxix, February, 1909. B.—First stage. A.—Second stage. Lateral anastomosis. Closed inverted ends of gut pointing in the same direction to allow extraperitoneal suture. (See Fig. 19.)

Intestinal Suture.—Figs. 17, 18 and 19 are taken from Fig. 6, A and B, and Fig. 7 from the ANNALS OF SURGERY, vol. lxix, p. 168, February, 1909. Fig. 17 (old No. Fig. 6B) shows the method of suture in which three rows of fine black silk are employed. In this figure the first row of sutures has been applied and the division of the gut on each side has been made through to the mucous membrane. The suture is the same way whether it is end-to-end, end-lateral, or lateral. In Fig. 18, all the posterior sutures have been applied, tied and cut. The artist in this case has not applied the first row of sutures properly. They should pass through the mucous membrane and be tied on the mucous-membrane side. He has drawn in only the second row. This method of suture was the original method of Billroth and is pictured in all his illustrations. I adopted it and have followed it with few exceptions throughout. The majority of surgeons today use catgut, especially for the mucous-membrane suture and the continuous suture. Many use catgut throughout. The object of this suture, as shown in Figs. 17 and 18, is to allow the two inverted ends of the gut to be placed extraperitoneally, as shown in Fig. 19 (Fig. 7 in ANNALS OF SURGERY). Then, if there is any leakage, it will be extraperitoneal.

I am going over carefully all the illustrations of tumors from cæcum to sigmoid. In gross pathology they showed the same characteristics of the few that we have already illustrated, and I shall leave their publication for Doctor Raiford's monograph. Only one will be selected to illustrate the point that some apparently inoperable tumors, even those that have had previous incomplete operations, may not only be operable but curable.

Apparently Inoperable Cancer of Colon.—Fig. 20. (Path. No. 28,918.) This mass, which consists of loops of adherent small intestines, a large bit of the abdominal wall, including the skin encircling the former scar, and the cæcum with the new growth, was excised at St. Agnes Hospital, in 1921. The patient was then given post-operative X-ray by my colleague Doctor Kahn. This patient is well today, 1932. In April, 1921,

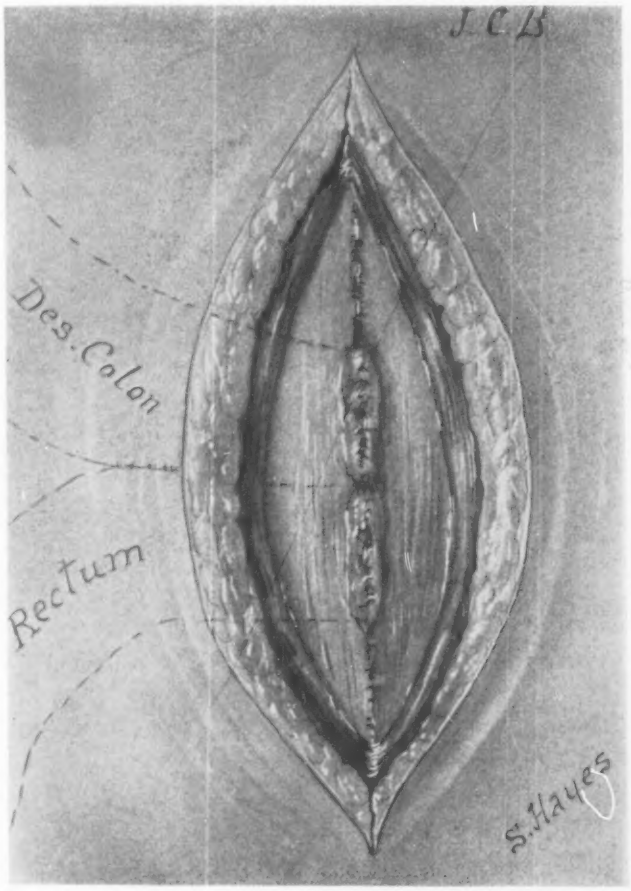

FIG. 19.—To illustrate the extraperitoneal position and suture of the two ends of the gut in the lateral anastomosis shown in Figs. 17 and 18 in the abdominal wound.

in this case the abdomen was opened on the diagnosis of appendicitis. The operator found what he thought to be an inoperable cancer of the cæcum. He removed a piece of the wall of the cæcum for diagnosis. It proved to be microscopically adeno-carcinoma, of a moderately low-grade malignancy. The operation of complete resection by me at St. Agnes took place five months after the exploratory operation. On admission to St. Agnes Hospital, he had a small fecal fistula, a palpable mass with induration of the abdominal wall.

When we opened the peritoneal cavity, there was no difficulty in picking out a piece

of ileum above the adherent loop, dividing it, closing the two ends, and then isolating the mesenteric vessels, until we reached the mesentery of the cæcum. Then we ligated these vessels in the mesentery until we explored the ascending colon and ligated it. When this was complete all we had to do was to remove the fistula, the scar, with a zone of skin, a wider zone of muscle and fascia. The adhesions on the outer side of cæcum and colon gave no difficulty. The complete separation of the mass and its removal required but an hour. A lateral anastomosis of the ileum and ascending colon was performed in the usual way. As we expected to bury the suture in order to fill the rent in the posterior peritoneum we covered the closed end of the colon by suturing the ileum and its mesentery to it. There was a considerable wound in the abdominal wall, but there was no difficulty

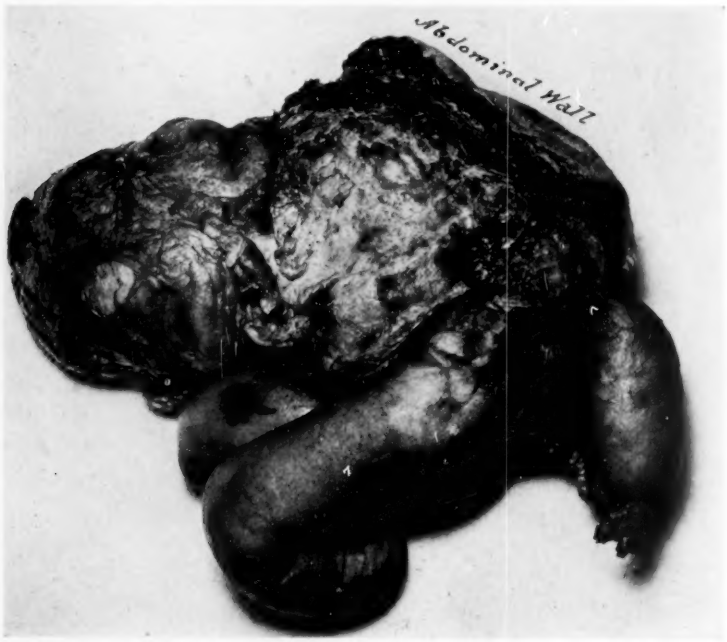

FIG. 20. (Path. No. 28,918.)—Photograph of loops of small intestine adherent to a cancer of the cæcum with the adherent wall of the abdomen completely resected in 1921. Well in 1932.

in closing off the peritoneal cavity. Much of the remainder of the wound was left open and drained. The tumor proved to be an extensive carcinoma of the cæcum and cancer tissue had grown into the abdominal wall itself and into the small intestine. But the glands showed no involvement. This patient has had no symptoms of recurrence or obstruction since the operation in 1921. Not infrequently has cancer of the cæcum assumed the clinical picture of chronic appendicitis. The palpable mass may be interpreted as adherent omentum about an infected appendix. In carefully studied cases the diagnosis of a condition other than appendicitis should be made. All operators must remember that in an exploratory operation on the diagnosis of chronic appendicitis when there is a palpable lump the possibility of a malignant operable tumor of the cæcum must be borne in mind.

SUMMARY AND CONCLUSIONS

Surgeons cannot with justice either to themselves or the public assume that their responsibility begins with the pre-operative preparation. The chief cause of failure to cure cancer of the colon and rectum is late intervention.

Contributory causes are incomplete pre-operative investigation in which the pre-cancerous or cancerous lesion is overlooked by some member of the medical profession and valuable time lost. The entire medical profession are apt to make the mistake of performing an incomplete diagnostic study before operation or an incomplete pre-operative preparation. Apparently the least factor in the failure to cure the majority of cases and cancer of the colon and rectum is the operative skill of the surgeon. This factor may be too large but it cannot be compared with the delay on the part of the patient and the failure to recognize an operable condition on the part of the general practitioner who does not keep up with modern diagnostic methods. Undoubtedly, in cancer of the rectosigmoid colon, surgeons of less experience and skill have too large a mortality. As I suggested in this paper, there should be no difficulty for them to recognize these cases clinically and back out gracefully either before any operation or after an exploratory laparotomy. In the latter event they can perform preliminary appendicostomy and save the patient much time.

I take the liberty of recommending appendicostomy preliminary to resection of every part of the colon except the right colon when the cæcum is removed. My impression is that lateral anastomosis, when possible, is safer than end-to-end. When the colon itself must be resected, the safest method of anastomosis, if it possibly can be done, is illustrated in Figs. 17, 18, and 19. In tumors of the rectum and rectosigmoid pathological studies and final results demonstrate that it is unnecessary for a cure to give the malignant tumor of the colon or rectum such wide margins of gut. The restricted operation should be chosen when possible, if it promises lessening of the operative risk. For the same reason, operation in stages should be chosen and blood transfusion freely employed. Do not wait for symptoms of shock —anticipate the collapse. Also, it should be remembered that the rectal tumor can be properly removed through the sacral route. It is perfectly possible to perform an abdominal colostomy if the sacral one is unsatisfactory. Many of our most experienced and best-trained diagnosticians often curtail the pre-operative diagnosis the moment something definite is found indicating surgical intervention. Many experienced surgeons do not give the patient before operations upon the colon proper pre-operative preparation. If there is obstruction, colostomy is indicated, which can be part of a pre-operative diagnosis and preparation, because the obstruction must be relieved. I recommend appendicostomy without exploration to determine the position of the tumor unless there are definite symptoms indicating the necessity of further exploration.

BRIEF COMMUNICATIONS

SOME SUGGESTIONS IN EXPERIMENTAL SURGERY

I. TECHNIC FOR OPENING AND CLOSING THE THORAX

II. SIMPLE METHOD FOR THE TRANSPLANTATION OF THE URETER AND THE COMMON BILE-DUCT INTO THE INTESTINE

(I) *Technic for Opening and Closing the Thorax.*—In many research investigations an important part of the operative procedure is a certain type of surgical manipulation within the cavity of the thorax. Although such procedures in experimental work have been common since Carrel* reported his first successful experiments, a simple and satisfactory method which can be employed in most laboratories is apparently not available. For several years we have used a technic for thoracic surgery which has proved to be very successful. The essentials of the method are: (1) an intercostal incision without resection of a rib, (2) wide traction with a strong, spreading retractor, and (3) strong sutures passing around each rib adjacent to the incision.

After the animal has been completely anæsthetized, and intratracheal artificial respiration has been started, it is placed on its side to expose the part of the thorax to be opened, a wide area of this side of the thorax having been shaved, washed with a fat solvent, and painted with two coats of 2 per cent. iodine in ether. The usual sterile linen is used for draping the animal, and the strictest asepsis is maintained at all times.

The interspace in which incision is to be made varies with the thoracic organs to be exposed. The first incision is made through the skin and subcutaneous tissue. The length of the incision varies with the size of the animal but should be large enough to permit good exposure. The edges of the skin are covered by towels, and the incision is carried on into the pleural cavity. A strong, self-retaining retractor is placed in position and the ribs are widely separated to permit easy access to the organs of the thorax. Any organ in the thorax can be approached with this exposure.

In closing the incision, interrupted sutures of heavy cobbler's thread are used for approximating the ribs; the sutures are placed about 2.5 centimetres apart, beginning well down in the angles of the wound. Each suture encircles the rib on each side of the wound. They are not tied until all are in place and the ribs have been drawn together with towel clips. The fascia and subcutaneous tissues are brought together with a running suture of No. 2 chromic catgut. When the first suture line has been completed, an artery forcep is inserted into the pleural cavity and opened. The air is then completely blown out of the thorax by increasing the intrapleural pressure, and the forcep is quickly withdrawn. The second suture line of catgut is

* Carrel, Alexis: On the Technic of Intrathoracic Operations. Surg., Gynec., and Obst., vol. xix, pp. 226–228, July, 1914.

then completed. Linen is used for closing the skin. A single layer of gauze, covered with collodion, is the only dressing used. Stitches are not removed unless they become infected.

(II) *The Transplantation of the Ureter and the Common Bile-Duct into the Intestine.*—Many methods have been devised for transplanting the ureter into the large intestine. Most of these we have tried experimentally. Although we have been successful, occasionally, in obtaining function of the kidney with each method, the percentage of satisfactory operations has not been high. Failures may be attributed to two main causes: the complexity of the technic, and the thickness of the muscularis of the large intestine of the dog. However, after various experiments, we finally adopted a simple

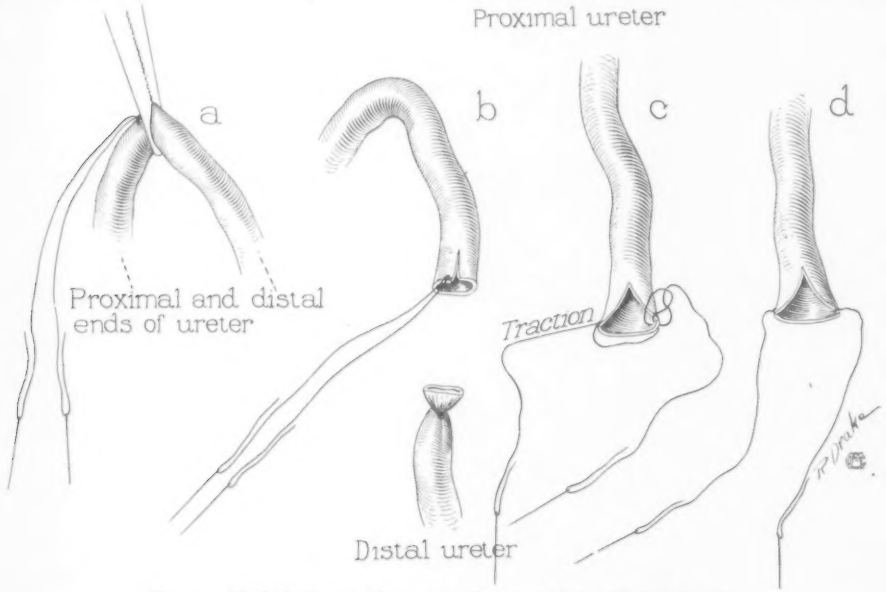

FIG. 1.—Method of preparing ureter for transplantation into bowel.

and satisfactory technic. We are presenting it here since it may be of value to experimental workers who desire a simple method for transplanting the ureter or similar structures.

Preparation of Ureter.—We shall describe the technic for transplantation of the ureter since it is the structure most often transplanted. However, the same technic is applicable for transplantation of the common bile-duct and the pancreatic duct.

The ureter is lifted with an aneurism needle and clamped with a small artery forcep as near the bladder as possible. While the ureter is held up with the forcep a suture of fine silk (No. 0) threaded with two needles (No. 12) is placed in the anterior surface of the proximal segment, close to the forcep (Fig. 1, *a*). This suture is tied and used for traction while the ureter is being cut proximal to the forcep. The distal segment of the ureter is tied with catgut and allowed to drop back. The proximal end of the ureter is held up with the suture and its end split for a distance of about one

centimetre as close to the suture as possible (Fig. 1, *b*). One end of the suture is held while the other is passed behind the ureter and inserted through the wall, into the lumen at the opposite corner, then out again, and locked (Fig. 1, *c*). Thus, when traction is made on each end of the suture, the corners, made by splitting the end of the ureter, are held wide apart (Fig. 1, *d*).

Preparation of Bowel.—At a point on the rectum easily approximated by the ureter, two mattress sutures of fine silk are placed parallel to each other and separated by about the width of the ureter. These sutures are placed slightly diagonal to the long axis of the bowel, so as to correspond to the normal course of the ureter as it will enter the bowel. The rectum is then

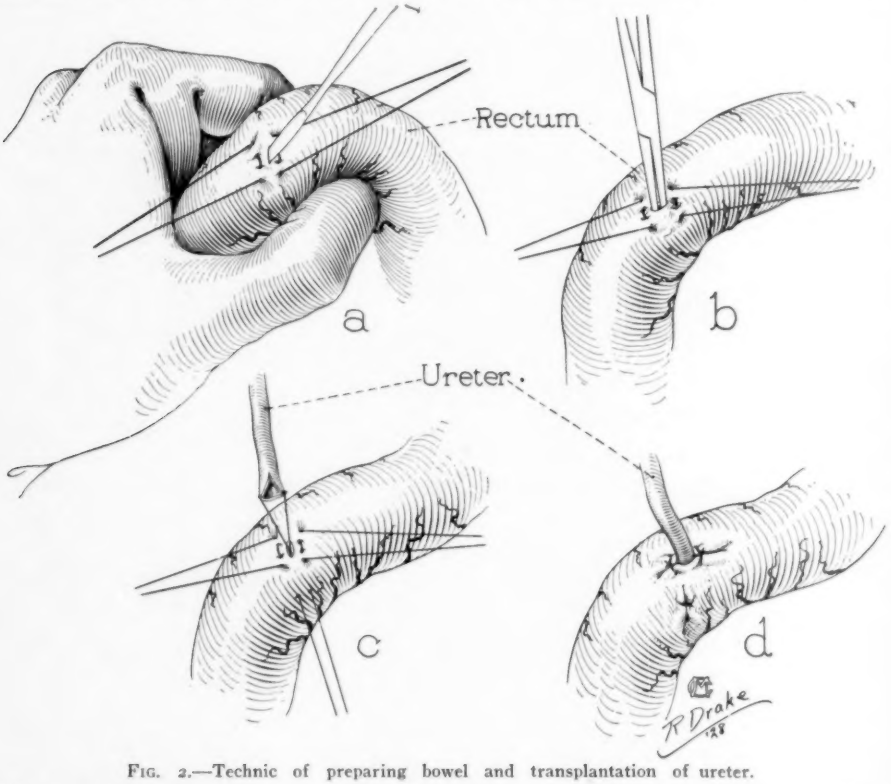

FIG. 2.—Technic of preparing bowel and transplantation of ureter.

lifted and a stab wound is made directly between the two mattress sutures (Fig. 2, *a*). A small mosquito forcep is inserted through the stab wound and the blades separated slightly to allow the mucosa to pout up through the wound (Fig. 2, *b*).

Implantation of Ureter.—The two needles, attached to the previously prepared ureter, are now taken one at a time and passed through the stab wound into the lumen and out again through the wall of the bowel about two centimetres beyond the stab wound. These are inserted in such a way that the split end of the ureter is brought against the wall of the bowel. Traction on these sutures draws the ureter into the lumen of the bowel, and when

they are tied it is held firmly in place (Fig. 2, *c*). The mattress suture on each side of the ureter is then tied, which causes dimpling of the wall of the bowel, inverts the mucosa and holds the ureter firmly.

Results following this simple procedure have been very satisfactory. Some of our animals have lived for several years with transplanted ureters and others with transplanted common bile-ducts. We have found, however, that the kidney is rarely normal after transplantation of its ureter, regardless of the method used. The liver also shows definite lesions after transplantation of the common bile-duct. On the other hand, the transplantation of the pancreatic duct is almost always successful and the gland usually remains normal.

MEREDITH G. BEAVER, M.D., AND FRANK C. MANN, M.D.,
of Rochester, Minnesota.
From the Division of Experimental Surgery and Pathology of The Mayo Clinic.

AN APPARATUS FOR CONTINUED ADMINISTRATION OF FLUIDS INTRAVENOUSLY*

IN 1924, Matas administered fluids intravenously in the treatment of patients following operation to help to ward off shock, toxæmia and exhaustion, and in order to replace slowly the fluids which had been lost by dehydration. Since that time many types of apparatus have been devised for the intravenous administration of fluid.

The apparatus I am describing, unlike many that are used in the gravity methods, is not expensive, and it can be assembled from tubing and bottles found in almost any laboratory. It consists of a bottle of a capacity of about 2 litres with graduations in 50 and 100 cubic centimetres (Fig. 1); two right-angle bent glass tubes, one long and one short; a long-stemmed funnel; a Murphy drip bulb without a hole for air; about four feet of rubber tubing, and an intravenous needle. The two pieces of bent glass tubing and the long-stemmed funnel are inserted through a rubber stopper (Fig. 1, *a*) which fits tightly into the neck of the bottle. The stem of the funnel and the long arm of the longer bent tube, *b*, pass to the bottom of the bottle. The shorter right-angle tube projects only a short distance within the neck of the bottle. The other arm of this shorter right-angle tube has a small fusiform enlargement into which cotton may be packed; it thus acts as a vent to admit air but will not allow contamination of the content of the bottle. To the shorter arm of the longer bent glass tube is attached a piece of rubber tubing about one foot long, of the type which is ordinarily used in administration of fluids intravenously. At the other end of this piece of tubing is attached a drip bulb, *c*, which does not have a hole in it to admit air. A second piece of rubber tubing runs from the lower end of the Murphy drip bulb to the needle by which the fluid is to be administered. The needle may be of the ordinary intravenous type, with any of the modifications which are recorded in the

* Submitted for publication October 22, 1931.

literature of today; for instance, it may be a gold needle which does not corrode easily. It may have a shield for support, and, as has been suggested by Matas,[2] it may have lateral openings in its shaft as well as the terminal opening; this latter feature is an added advantage although not wholly necessary.

The bottle, the tubing, and the needle are sterilized in an autoclave. The fluid to be used is then poured into the bottle through the long-stemmed funnel. A piece of sterile gauze is placed over the funnel and held in place by a rubber band. Because the apparatus works by means of a siphon, a bulb, *d*, is used to set the fluid in motion. The bulb is of the kind commonly

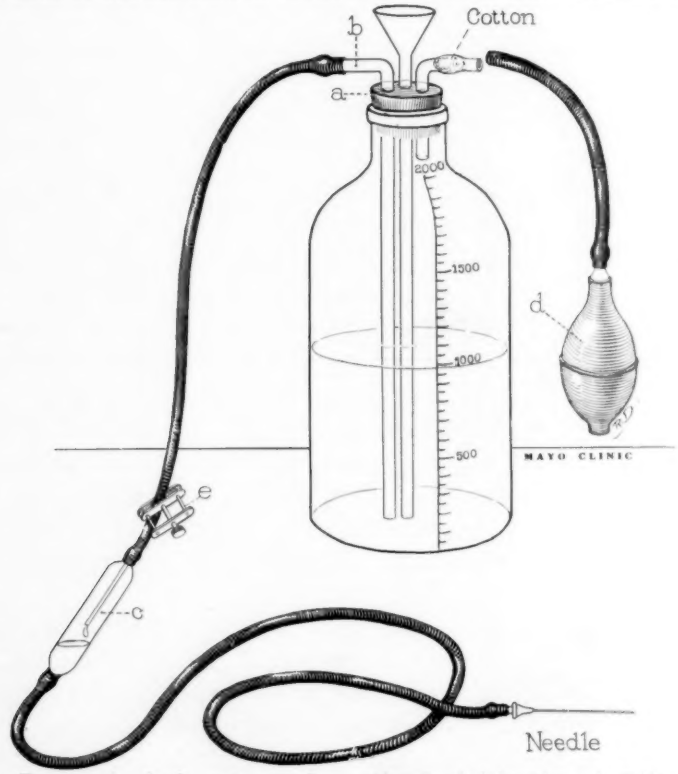

FIG. 1.—A simple apparatus for continued administration of fluids intravenously.

used in any apparatus for testing blood-pressure. This is attached to the small, right-angle tube, and slight pressure is exerted on the bulb, causing the fluid to rise in the funnel and in the long right-angle glass tube. Since the tube is at a lower level than the funnel (Fig. 1), the fluid soon spills over and runs out of the drip and distal end of the tubing to the needle. The bulb is then disconnected, leaving the smaller glass tube as an air intake. The bottle is placed at a level of about one foot above the forearm or leg into which the fluid is to be injected so that the fluid may flow more readily, aided by gravity. The needle is then inserted into the vein, choosing a place on the limb which is relatively free from motion. The needle is strapped in

place by means of adhesive tape placed across its shaft, above its point of insertion. A small piece of sterile gauze is fastened so that it rests over the point of insertion of the needle. The tubing is also fastened to the limb for a distance of about 6 to 8 inches proximal to the point where it is connected to the needle. If a place has been chosen well away from a region where there is motion, as near a joint, there is no need for further immobilization of the limb. If, however, it has been necessary to choose a vein close to a joint, it may be wise to immobilize the part while the apparatus is in use. A very efficient method for immobilization is wrapping an ordinary pillow around the limb.[1] This prevents motion and is much less tiresome than a firm splint. The apparatus is set running at about 50 to 60 drops for each minute and can be left unattended for a considerable time. The rate of flow through the drip is controlled by a small clamp, *e*, which is placed just above it. A warming device, as a hot-water bottle, may or may not be used. It has been shown that fluids can be given slowly at room temperature without ill effects. Three to four days has been about the longest period found necessary to use the same vein. It is often well to open the clamp on the tubing about every six to eight hours in order to allow the fluid to run more rapidly and to prevent stasis, which encourages the formation of thrombus around the point of the needle.

The apparatus has proved satisfactory in administration of a large amount of fluid within a short time. From 5,000 to 6,000 cubic centimetres or more may be given in twenty-four hours with little, if any, discomfort. It is well known that patients frequently experience much discomfort from the hurried administration of 1,000 to 2,000 cubic centimetres of fluid.[3]

The apparatus has been used effectively also for continuous lavage of the bladder after operative procedures to keep the bladder free from blood-clots.

STANFORD W. MULHOLLAND, M.D.,
of Rochester, Minnesota.
Fellow in Surgery, The Mayo Foundation.

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[3] Penfield, W. G., and Teplitsky, David: Prolonged Intravenous Infusion and the Clinical Determination of Venous Pressure. Arch. Surg., vol. vii, pp. 111–124, July, 1923.

HÆMORRHAGE INTO A PITUITARY TUMOR FOLLOWING TRAUMA

THE question of the relationship of trauma to the initiation or aggravation of all types of disease is one that is more and more demanding the attention of physicians and industrial boards. Where the pathological processes that may follow trauma are clearly understood, court decisions and awards to

workmen are, as a rule, well standardized. Where there is little information regarding the pathological processes that may follow in the wake of trauma, medical as well as court decisions are at great variance, disputed, and often proven incorrect by subsequent events or the lapse of time.

So clearly seems the relationship of trauma to hæmorrhage into a pre-existing pituitary tumor or cyst in a workman recently seen that it may be of interest to call attention to the possibility of this. Description or pathological material itself demonstrating traumatic hæmorrhage into brain tumors in general is very meagre. Still more rare are specimens of hæmorrhage,

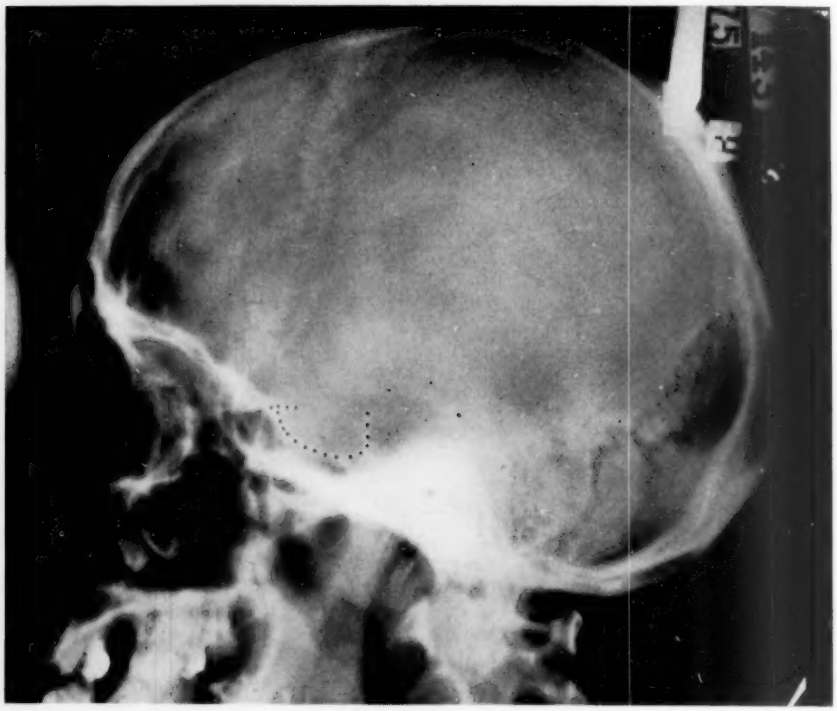


FIG 1.—X-ray of skull showing much enlarged sella turcica.

traumatic in origin, into pituitary tumors. Spontaneous hæmorrhage into pituitary tumors must, however, be fairly common as an accompaniment of degeneration of tumor tissue. Hæmorrhage into normal pituitary gland tissue following severe trauma such as fracture of the skull is fairly well known. Cushing illustrates one case and quotes another where marked hypopituitary symptoms followed severe head injury.

The author has seen in Doctor Cushing's clinic an instance of aggravation of ocular symptoms associated with a pituitary tumor which followed a blow over the temporal region. At operation the tumor was found to be largely destroyed by hæmorrhage into its substance. Doctor Cushing has kindly

permitted me to refer to this case and also to a specimen in his collection of an extensive infiltration of blood into a pituitary tumor following trauma. At autopsy this seemed to be the sole cause of death. This hæmorrhagic infiltration into the pituitary tumor followed a fall. A review of the literature (by title) on pituitary tumors for the past twenty years fails to reveal any contributions on this subject.

CASE.—E. C., hospital No. 45075. The patient, aged twenty-eight, was referred to the Strong Memorial Hospital by Dr. T. H. Farrell, of Utica, New York, because of blindness of the left eye and failing vision in the right. His past history was entirely irrelevant. The patient repeatedly stated that he had never had any disturbance of vision prior to the present illness.

In September, 1930, some five and one-half months prior to entry, the patient was struck in the left eye by a fist. He was "dazed" for a few moments but did not have any other general symptoms. The periorbital tissues became rapidly swollen and ecchymotic and the lid could not be opened for two or three days. So far as he is aware the sclera or conjunctiva itself was not discolored. When the patient was again able to open the left eyelid he noted a marked blurring of vision on the left. Total blindness in the left eye ensued, in about five to six weeks. Vision in the right eye was then noted to be less acute than formerly. He himself noted that vision in the temporal field was gradually being encroached upon. This progressed steadily until he had a complete loss of temporal field vision and probably central vision as well.

At no time did he experience any headache. There likewise have not been any "neighborhood" symptoms. Sexual powers, never very great, had not been altered.

There was not to be obtained a history of symptoms suggesting that he had had a subarachnoid hæmorrhage at the time of the injury. He was a well-developed and nourished male who had none of the usual appearances of acromegaly or marked hypopituitary disease. The skin was normal in texture. Distribution and amount of hair were not unusual.

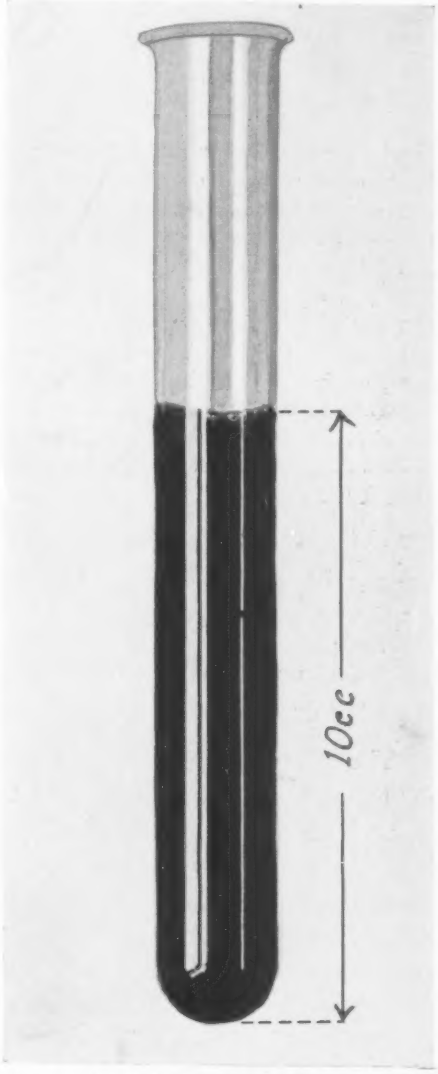


FIG. 2.—Actual size drawing of test tube containing fluid from pituitary cyst.

Neurological examination was entirely within normal limits except for the ophthalmological examination. Both pupils were dilated, equal and round. Pupillary reaction to light was absent on the left side, the right side being normal. Light stimulus to the right retina was associated with contraction of the left pupil. The reverse was not

true. Extraocular movements were normal. Both optic nerve heads showed fairly marked pallor. It was more marked on the left, however. Visual fields showed a complete loss of vision on the left. The central vision as well as the temporal field vision on the right had been lost. Visual acuity was 20/200 on the right side.

X-rays of the skull showed a marked enlargement of the sella turcica with erosion of the posterior clinoids and a thinning out of the floor of the sella. (Fig. 1.) X-rays of the hands were taken for a question of "tufting" of the terminal phalanges but none was demonstrated.

Laboratory examinations were within normal limits. The urine was normal in amount and gravity (1020). Blood smears and blood counts were normal. Basal metabolic rate was −18 per cent. A sugar-tolerance test showed a normal curve. Fasting blood sugar was 70 milligrams per 100 cubic centimetres. One hundred grams of glucose were given by mouth. A blood-sugar reading one-half hour later was 130; one hour—120 milligrams; one and a half hours—68 milligrams; two and a half hours—70 milligrams; three hours—100 milligrams.

Operation.—A right frontal craniotomy was performed under local and ether anæsthesia. The dura was cut along the great wing of the sphenoid on the right side and the region of the pituitary gland exposed without difficulty. The right optic nerve was identified and seen to be quite flattened by a tumor mass beneath it. The left optic nerve could not at first be seen. A needle was introduced into the substance of the tumor and about 10 cubic centimetres of chocolate-brown fluid aspirated. (Fig. 2.) The walls of the cyst collapsed at once. The left nerve could then be easily seen stretching like a thin ribbon over the capsule of the tumor. The top of the cyst wall was removed for a specimen.

The cystic fluid was examined for remnants of tumor tissue but none could be identified. Cholesterin crystals in the fluid could not be made out on microscopical examination.

The post-operative course was uneventful. Vision in the left eye remained nil during the hospital stay. The visual field on the right side widened out so that central vision was present and acuity had returned to 20/60.

The enlargement of the sella turcica shown by X-ray would seem to be far more than could have taken place in a period of five to six months. In all probability the patient had a very slowly growing tumor that may have been present for years. The lack of headache at any time prior to injury would also argue for its slow growth. Whether or not this had been large enough to cause any visual-field impairment is impossible to say. An ophthalmological examination had never been done prior to injury and the patient's powers of observation seemed less than average.

Conclusion.—Hæmorrhage into a pituitary adenoma or cyst following trauma, though rare, is a real possibility and may well be kept in mind in considering the differential diagnosis of optic atrophy following head injuries.

WILLIAM P. VANWAGENEN, M.D.,
of Rochester, N. Y.

From The Department of Surgery, Neurosurgical Division of the University of Rochester.

COMPLETE FORWARD DISPLACEMENT OF THE PERONEAL TENDONS DUE TO CALLUS

So FAR as can be learned from reference to the literature, complete forward displacement or dislocation of the peroneal tendons is rare. As a sequence to callus formation after fracture of the os calcis, this condition has never been reported so far as we can determine.

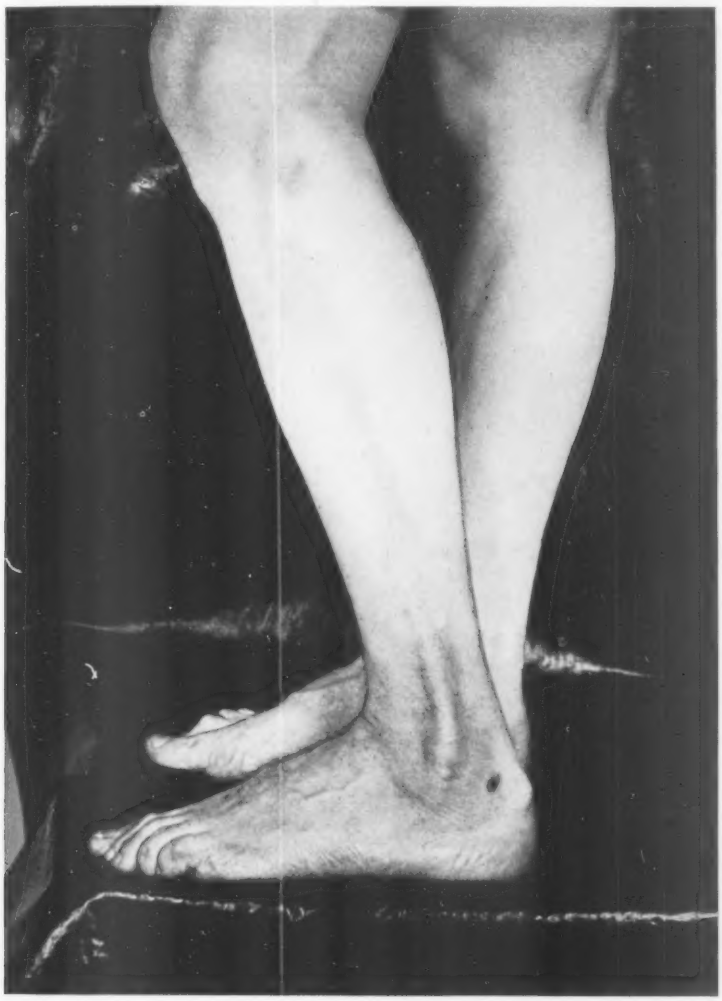


FIG. 1.—Lateral view, showing the complete forward displacement of the peroneal tendons.

Cotton[1] and Magnuson[2] have each reported a series of old fractures of the os calcis that were operated upon because of one or a combination of the following causes of disability: (1) A resultant traumatic flat foot, *e.g.*, pronation of the foot and strain on the plantar fascia; (2) loss of lateral

[1] Cotton: ANNALS OF SURGERY, vol. lxxiv, p. 294, September, 1921.

[2] Magnuson: Jour. Am. Med. Assn., vol. lxxx, p. 1511, May, 1923.

motion, and (3) excess callus formation—posterior to and beneath the external malleolus. The latter disability was the cause of the forward displacement of the peroneal tendons in the case herewith reported. In their series of cases, neither Cotton nor Magnuson reports finding such a condition previous to or at the time of operation. Magnuson states that "in excess callus formation the peroneal tendons either have been forced entirely away from behind the external malleolus and are held tightly under their pulley ligaments in the groove between the two structures or are caught between the callus and the external ligaments." (Fig. 1.) In Fig. 2, a diagrammatic sketch of our case, can be seen the complete forward displacement of the tendons by the callus formed at the fracture site.

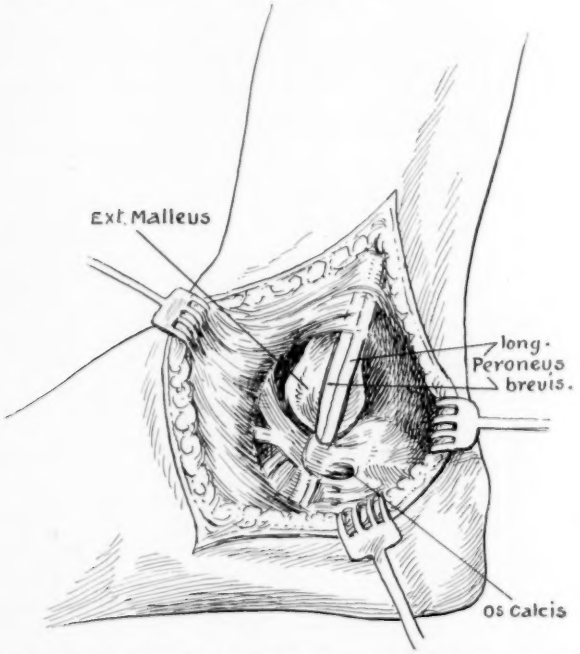


FIG. 2.—A diagrammatic sketch showing the complete forward displacement of the peroneal tendons due to callus formation.

CASE REPORT.—A middle-aged man fell from an eight-foot scaffold, landing on his heels on a concrete floor. Röntgenographical examination showed a comminuted fracture of the left os calcis. The foot and leg were put up in a Böhler screw traction apparatus and a plaster case was applied. A fairly good result was obtained, but after nine months the groove posterior to and beneath the external malleolus had largely filled with callus displacing the tendons. (Figs. 1 and 2.)

There is a very apparent widening of the ankle entirely due to the forward displacement of the peroneal tendons until they occupy a position in front of the external malleolus.

The removal of the excess callus and replacement of the peroneal tendons was done after the technic of Magnuson.

EDWARD P. HELLER, M.D.
CARROLL P. HUNGATE, M.D.
Kansas City, Mo.

HEPATICO-GASTROSTOMY

THE operation of anastomosing the hepatic duct with the stomach has been done only in a limited number of cases. Nature, in a few instances, has performed the operation of cholecystogastrostomy herself when the presence of a gall-stone in the gall-bladder has set up a pericholecistitis with adhesions of the fundus to the stomach. The gall-stone has then ulcerated through the walls of the stomach, thus producing a biliary fistula allowing the bile to pass directly from the liver into the stomach via the hepatic duct and gall-bladder. Deaver, in his Surgery of the Upper Abdomen, 1914, cites the following case: "Upon opening the abdomen, found duodenum and pylorus bound by strong adhesions to fundus of gall-bladder and lower surface of liver. On releasing adhesions, a perforation of stomach and of gall-bladder was found with a large gall-stone protruding into stomach."

Various methods have been employed for connecting the hepatic duct to the intestines when the gall-bladder and common duct have been removed, either because of cancer or traumatism.

Hepaticostomy was first done by Kocher, in 1889, when he sutured the stump of the hepatic duct to the skin for the purpose of drainage. The patient lived seven days. A similar operation was made by Sendler, which he called hepatostomy, wherein the hepatic ducts were entirely occluded, thus preventing any bile being excreted. In this case, the dilated intrahepatic bile channels projected from the surface of the liver in the form of small cysts. Sendler introduced a trocar into one of these cysts, inserted a drainage tube, brought the tube to the surface and stitched it to the skin—thus he established liver drainage.

It was Hildebrandt who introduced the operation of cholecystogastrostomy, and was therefore the first surgeon to demonstrate that the presence of bile in the stomach produced no bad effects. That operation has been done many times since. Various operations have been devised and successfully performed for anastomosing the hepatic duct with the intestines, either duodenum or jejuneum—hepatico-enterostomy. These methods, however, have the common objection that infection is likely to travel upward from the intestines.

There is no record earlier than 1914, which the writer has been able to find, wherein the hepatic duct has been implanted directly into the stomach.

Deaver, in his work of that year, says:

"The use of the jejunum in such circumstances (hepatico-enterostomy) is objectionable, but if an anastomosis can be made with the stomach this should be done." But he mentions no instance where it had ever been done, save one Wilms (Brandt, *ibid.*, Fall 4) where a biliary fistula resulted from an injury to the common duct at a previous operation. Three succeeding operations failed to correct the fistula. In a fourth operation, he connected the hepatic duct to the stomach by a rubber tube which was subsequently vomited, necessitating a fifth operation. This was successful.

Since 1914, a number of hepatico-gastrotomies have been reported with varying degrees of success. Tschassownikoff (Zur Frage über die "hepato-Cholangiogastro-bzw. enterostomia"—Operation. [Hepato-cholangiogastro or enterostomy.] Zentralblatt fur

Chirurgie, vol. li, pp. 2082–2083, 1924) reports a case wherein he prefaces his report of the case in these words. "This operation belongs to the very rare operations, and is only employed in congenital, benign or malignant occlusion of the hepatic duct, as soon as one does not succeed in removing the obstruction by way of the porta hepatis.

"This operation, 'cholangiogastrotomy,' was performed in the surgical clinic of Odessa in order to close a biliary fistula, and to remove an impermeability of the ductus hepaticus."

In the Journal of the American Medical Association, April 14, 1931, Waltman Walters, Rochester, Minnesota, presents an article under the head of Complete Stricture of the Common and Hepatic Ducts, Treated by Transplantation of the External Biliary Fistula into the Stomach or Duodenum. In this article, the author quotes W. J. Mayo, who, in 1905, made an accurate anastomosis between the stump of the common duct and the duodenum. Dr. F. H. Lahey reports in the ANNALS OF SURGERY, June, 1923, of establishing an external biliary fistula for duct obstruction, and subsequently transplanting this fistula into the stomach or duodenum.

Dr. Howard Lilienthal reports a similar operation, ANNALS OF SURGERY, June, 1923, and Hugh Williams also reports his method of transplanting a biliary fistula into the first portion of the duodenum.

Walters has collected only twelve cases of successful transplantation of biliary fistulæ into stomach or duodenum.

Wickhoff and Angelsberger (Berlin klin. Wchnschr, vol. vi, p. 138) were the first to perform cholecystogastroenterostomy, Jacobson having collected seventeen cases of this nature from literature. But in all these cases the gall-bladder was employed to make the anastomosis.

The object in reporting the following case is: First, because it presents some interesting features relative to obtaining temporary relief from so distressing a condition as advanced cancer of the gall-bladder and common duct; and, second, to show the priority, so far as any literature shows, of the method employed. Up to the date of this operation, 1914, it had not been demonstrated conclusively that bile flowing continuously and directly from the liver into the stomach would cause no serious disturbance to the latter; second, that when the bile is so delivered it functions just as normally as when emptied into the intestine; third, that during the period of fifty-four days from the establishing of a fistula from the hepatic duct to the surface of the skin, there was no appreciable disturbance of digestion, although not a particle of bile was flowing into the intestine.

The case is as follows:

Mrs. P., aged seventy-six years, widow, one child. Mother died of "shock" at advanced age, had been an invalid for two years prior to death suffering from dysentery. Father died of "bowel trouble" at eighty years of age.

Previous health of patient, good; no serious illness; had one attack of "bowel trouble" which was of short duration. Said she occasionally had bilious attacks. Had led a very active life. She was deeply jaundiced, stools clay-colored, urine highly bile-tinged, tongue coated—complained of constant pain upper right quadrant, but never had had pain of biliary colic type; marked fatigue; no temperature; emaciation; no appetite.

A distinct tumor in the upper right quadrant could be palpated. It was not markedly sensitive to pressure.

With the hope of giving temporary relief, the patient was taken to the Deaconess Hospital, Boston, and operated on April 25, 1914.

A right lateral incision disclosed a cancerous mass involving gall-bladder, glands and common duct to within a short distance of the ampulla. The gall-bladder, the cystic

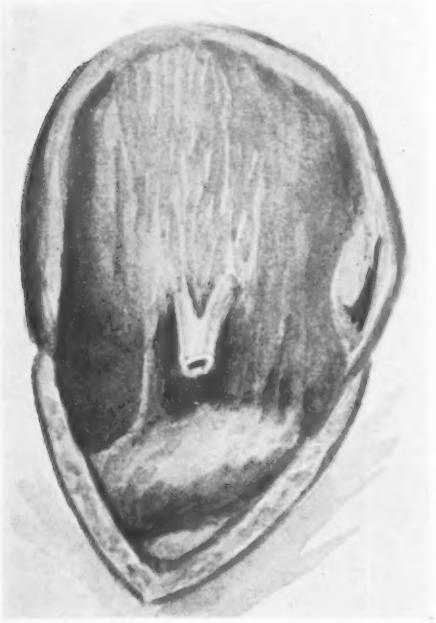


FIG. 1.—The gall-bladder and common duct have been removed. The short stump of the hepatic duct protrudes from the liver.

FIG. 2.—A rubber drainage tube has been sutured to the stump of the hepatic duct and the free end brought out of the incision.

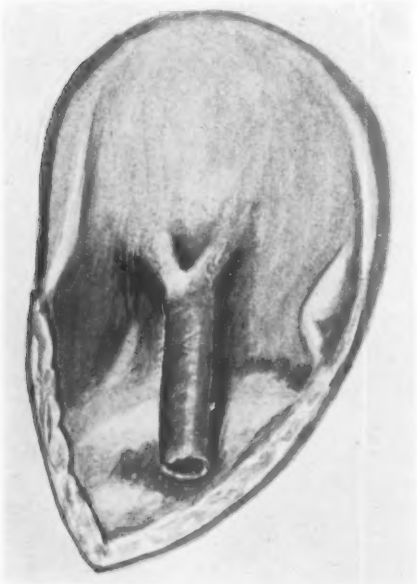


FIG. 3.—Fifty-four days later. The fistulous tract left after removal of the rubber tube appears in an elongated hepatic duct.

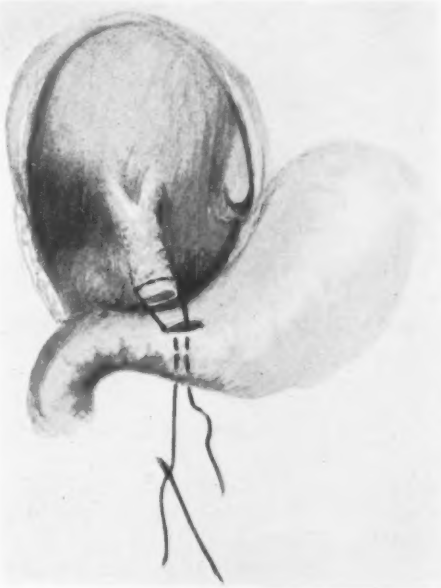


FIG. 4.—Button-hole opening made in stomach wall near pylorus. Stomach transfixed with sutures for the purpose of drawing the elongated duct into the button-hole opening.

duct and the greater part of the common duct, together with involved glands, were removed. The removal of the above-mentioned structures left a short end of the hepatic

duct protruding from the liver, and the remaining portion of the common duct. (Fig. 1.) From the stump of the hepatic duct clear bile was seen flowing. Over this hepatic stump a rubber drainage tube was sutured (Fig. 2), brought to the surface, a tissue drainage inserted alongside of the rubber tube leading down to the duct. The remaining portion of the common duct was ligated near the duodenum. The incision was then closed. Before the dressings were applied, bile was already flowing from the rubber tube.

Patient made a good recovery and left the hospital much improved. The rubber tube was removed at the end of two weeks. Her jaundice had practically cleared up, urine normal, but of course her stools were still clay-colored, as it was not possible for any bile to find its way into the bowel.

By June 18 she had improved to such an extent that it was deemed best to make an attempt to divert the bile from the rubber drainage tube into some channel whereby it could reach the intestine. She was again taken to the Deaconess Hospital and a second operation was done. Nature had constructed a very satisfactory fistula (Fig. 3) leading from the stump of the hepatic duct to the surface, which had acted perfectly in draining

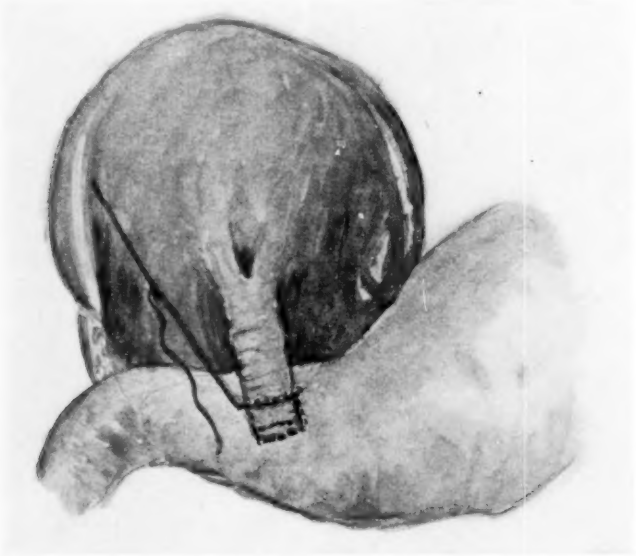


FIG. 5.—Elongated hepatic duct sutured into the stomach.

the bile from the liver. This fistulous tract was carefully dissected free from surrounding adhesions. The question next to be decided was to what structure should the fistula be anastomosed to get the best results. Fearing infection, should the connection be made either with duodenum or jejunum, the pyloric end of the stomach was chosen, particularly as that portion of the stomach lay in close proximity to the liver and some adhesions thereto had already been formed.

A buttonhole opening (Fig. 4) was then made in the stomach wall nearest the free end of the fistula. The stomach wall was then transfixed with a straight needle, threaded with linen, at a point opposite the buttonhole opening. The needle was made to emerge through this opening, the end of the fistula transfixed with the linen, and the needle made to emerge at the point of entrance; sufficient traction was then made to draw the fistula well into the stomach opening. (Fig. 5.) Here it was firmly sutured, a fold of omentum was laid over the suture line and stitched to the stomach wall for protection against leakage. The stomach was further anchored to the under surface of the liver, wound closed with drainage.

The patient made an excellent operative recovery. Drain removed in forty-eight

hours. Wound healed primarily. She vomited bile a few hours after she reached her room but none thereafter. On the third day there was a normal bowel movement, showing a distinct bile stain in the stool. No returning jaundice, good appetite, gain in strength. About July 10 she again showed signs of jaundice, although her stools had a good bile tinge. No vomiting and good appetite. There was every evidence that the anastomosis between hepatic duct and stomach was perfect, as the stools continued normal in color. She died August 14, 1914. No autopsy allowed. Cause of death given as metastasis into liver.

Thus the practicability of a hepatico-gastrostomy was established. If the operation has been performed in just this manner prior to 1914 no record of it has been found.

Boston, Mass. DEWITT G. WILCOX, M.D.

TRAUMATIC LATERAL DISLOCATION OF THE PATELLA

TRAUMATIC dislocations of the patella are seen rather infrequently. Even among industrial accidents, of which there are at present a large number, one rarely comes across an instance of dislocation of the patella that is not part of a more extensive and more serious injury to the knee. Four factors commonly predispose to an outward dislocation of the patella: (1) Laxity of the quadriceps muscle; (2) contracture of the iliotibial band and the external lateral patellar expansion of the quadriceps aponeurosis; (3) under-development of the lateral condyle of the femur, permitting abnormal outward mobility of the patella; and (4) outward rotation of the leg. Any one or all of these conditions may be involved in the mechanism of a given case of outward dislocation of the patella.

In my case, the patient had had anterior poliomyelitis, as a result of which he had a flexion deformity of the knee, weakness of the quadriceps muscle, shortening of all the soft tissues on the outer aspect of the knee and thigh, a marked knock-knee, and a fixed outward rotation of the leg. Therefore, a moderate trauma, caused by a fall, was sufficient to push the patella outward.

Dislocation of the patella is said to occur when the knee is in either hyperextension or flexion. In hyperextension the patella has been pulled up above the external condyle, which no longer acts as a barrier to outward movement of the patella. When the knee-joint is flexed the patella lies over the lower articular surface of the lateral condyle and can readily slip outward. In my patient the knee was continuously flexed. During the fall the joint became more flexed, so that the patella could be displaced.

My case has the further interest in that the patella was jammed against the condyle so tightly that it was virtually impacted in the femur. Though the patient was seen soon after the injury, manipulation under anæsthesia was not sufficient to reduce the dislocation. Even at the open operation considerable difficulty was encountered in dislodging the patella.

CASE REPORT.—Frederic C., colored, twenty-five years old, was admitted to the Hospital for Joint Diseases February 28, 1930. Five days previously he had fallen down five steps, striking the right knee. After getting up he found that he could neither

straighten nor bend the knee. The joint was painful, and soon after the injury it became swollen. At the age of seven years he had had an attack of infantile paralysis. Since then the right lower limb had been weak and atrophied. The knee was slightly bent and the leg was rotated outward. He was unable to bear weight on the right leg. The knee was enlarged, especially in the transverse diameter. The patella was absent in the front, but it was palpable on the lateral aspect of the knee. It was jammed up against the external condyle and was immovable. The iliotibial band was taut. There was a complete outward dislocation of the patella. In addition the patella was rotated 90° on a vertical axis, so that its articular surface was in contact with the lateral surface of the external condyle. The inner border of the patella was directed forward and caught in a groove in the femoral condyle.

Attempts to reduce the dislocation under gas-oxygen anæsthesia were not successful. Apparently the patella was caught in a groove under a ledge of bone, from which position it was impossible to dislodge it.

On the following day a median incision was made on the front of the knee from three inches above the upper border of the patella to the tubercle of the tibia. The synovial lining was found greatly congested and thickened. The patella was external to the condyle. Since the patella could not be pushed forward, a vertical incision was made into the capsule lateral to the patella. The knee was forcibly extended, whereupon the patella could be brought forward and inward into its normal relation with the femur. With the knee extended it was observed that the patient had a marked knock-knee deformity. This evidently contributed to the dislocation. The capsule of the joint was reefed by overlapping the inner margin over the outer. The margins of the capsule were held firmly together by numerous interrupted sutures of chromic catgut. The incisional opening in the outer part of the capsule was covered over with fascia. After the wound was closed, the knock-knee deformity was partly corrected by manual force and the limb was immobilized in a plaster-of-Paris bandage extending from the groin to the toes.

The post-operative X-ray picture showed complete reduction of the dislocation. The patient had an uncomplicated convalescence with return of an extensive range of motion in the knee.

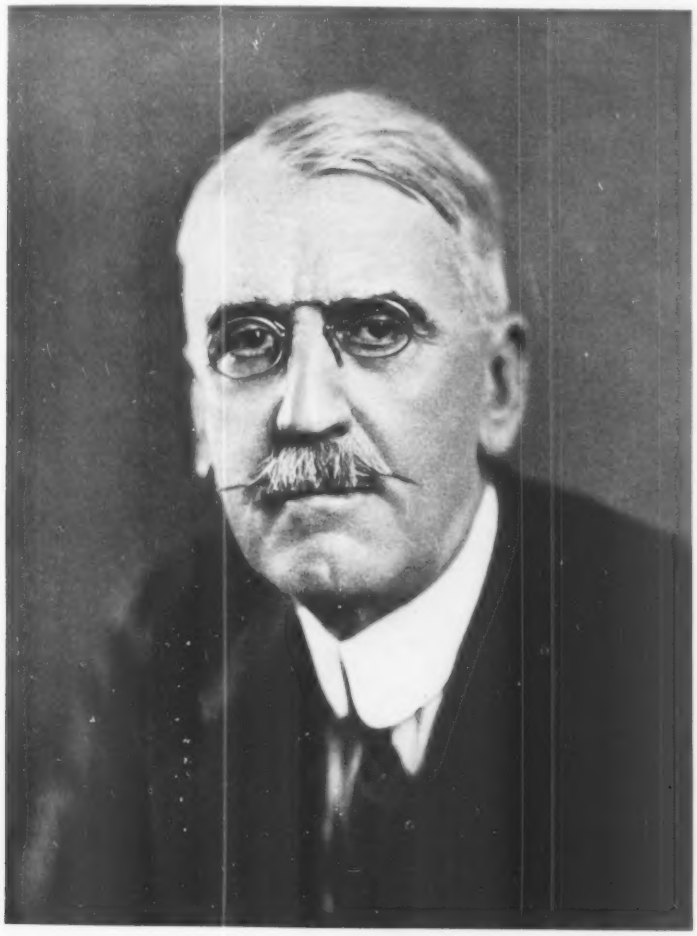
SAMUEL KLEINBERG, M.D.,
New York, N. Y.

MEMOIR

JOHN BLAIR DEAVER, M.D.

Born July 25, 1855–Died September 25, 1931

Dr. John B. Deaver was born in a small town in Lancaster County, Pennsylvania, where his father was a famous "country doctor," of Scotch-Irish descent. The son passed his entire professional life in Philadelphia, and died there, at the age of nearly seventy-six years; but, until within a



John B. Deaver, M.D.

few weeks of his death, "his eye was not dimmed nor his natural force abated." His death was due to an obscure anæmia for which he had submitted to numerous blood-transfusions but for which no cause was found at autopsy.

He was conscious, always, of his lack of an adequate pre-medical education. He received his degree of M.D. from the University of Pennsylvania

in 1878. He received the honorary degree of Sc.D. from Franklin and Marshall College, and that of LL.D. from Villanova College. He worked in the anatomical department of his *alma mater* from 1880 to 1899, conducting also large and very successful quiz-classes in anatomy and in surgery; but when, in 1899, his rival, J. William White, was given general charge of surgical instruction (during the last illness of Ashhurst), Deaver retired from the University until 1911, when he resumed teaching as Professor of the Practice of Surgery, succeeding White in 1918 as Barton Professor of Surgery. His tastes and abilities, however, were not adapted to professorial duties, and, though the age limit for retirement was twice extended in his favor, in 1922 he resigned all active duties at the university, retaining, however, until his death, the title of John Rhea Barton Emeritus Professor of Surgery.

Deaver became one of the surgeons to the German Hospital of Philadelphia in 1886, and soon made himself so secure in this position that the other attending surgeons were forced into the background, and in 1896 he was given the title of Chief of the Surgical Department, continuing thus, when at the time of the German war it was thought expedient to change the name of the German Hospital to that of the Lankenau Hospital, after its chief benefactor. At the German (afterwards Lankenau) Hospital, Deaver established his Saturday afternoon operative clinics, which became the Mecca for surgeons and students of surgery from all parts of the civilized world, and it is in connection with this clinic rather than with the university that his name will be remembered.

Coming to Philadelphia as a country youth, Deaver felt most attracted to Agnew, who also came to Philadelphia as a country youth from Lancaster County; and his career was to a large extent modelled on that of this master surgeon. In his later years Deaver became much more robust and looked like a prosperous business man or banker. Deaver was regarded as a *radical* in his early years, and he was proud to maintain this reputation to the last. Only "the aseptic scalpel" of the surgeon, he maintained, could properly attack the many hidden lesions, especially those of the abdomen, which his own work did so much to bring to notice. He was among the earliest and most valiant champions of immediate appendectomy for acute appendicitis. He created the phrase "an inch and a half, a minute and a half, a week and a half" to indicate the length of the incision, the duration of the operation, and the stay of the patient in the hospital, when early operation was employed.

As an operator, Deaver was rough, ready and radical—a great "slasher." He utterly lacked the patience required for the finer manipulations of many operations, but, in the abdominal cavity, he felt unbounded self-confidence, and met accidents (which sometimes occurred) with perfect poise and ready wit. As he grew older he became a little more cautious, and did not hesitate to declare some cases "inoperable." Though, like Agnew, an excellent anatomist, he never became a really skillful dissector. His work at the university in Applied Anatomy was really operative surgery and had only

the most incidental connection with the applications of anatomy to medicine or surgery. He was actually less skillful with his fingers than was his friend and classmate Harte; but he was a better teacher, by telling phrase and lucid demonstration holding throngs captivated hour after hour in his clinic, where he was not wholly averse to "playing to the gallery." Among his favorite catch phrases may be recorded "cut well, get well, stay well," comparing the permanent results of operation with the frequent recurrences encountered after non-operative treatment; and, in relation to officious after-treatment, his frequent plea to his resident physicians to "let the patient get well." He is also largely responsible for that anathema of modern diction, the use of the word "pathology" instead of pathological lesion.

Thus he would ask: "What is the pathology"; and he would even demonstrate as "the pathology," the lesions uncovered by operation, not understanding that *pathology*, being the science of disease, exists not in the patient but only in the brain of the surgeon.

Though Doctor Deaver found his inability to write English correctly a great handicap, he was not thereby deterred from his ambition to shine as an author; but, like Agnew before him, by associating with himself younger men possessing an adequate pre-medical education he was enabled to appear before the profession as the author of numerous monographs and text-books and of innumerable pot-boilers in the form of addresses on topics of ephemeral if current interest. He was widely sought throughout this country north, east, south and west, as a contributor to State and County Medical Society programs, and he rarely declined these invitations, feeling, as he said, under certain obligations to the physicians who sent their patients to his care. Among his more important monographs should be mentioned:

Appendicitis (1896); 4th edition, 1913.
Surgical Anatomy, 3 vols., 1899–1903; 2nd edition, 1926–1927.
Surgery of the Prostate (1905); 2nd edition, 1922.
The Upper Abdomen, 2 vols., 1909–1914; 2nd edition, 1921.
The Breast, 1917.
Excursions into Surgical Subjects, 1923.

Doctor Deaver probably did more operations than has any surgeon in Philadelphia, either before or since his time, though he once said to the writer of these lines "there is no doubt that your father did more operations than anyone else in Philadelphia ever did—why, *he was operating all the time!*"

Deaver's phenomenal physique enabled him to maintain his health and strength in spite of advancing years. He reckoned among the valuable possessions of a surgeon not only those demanded by Lord Moynihan (*the eye of an eagle* and *the hand of a woman*), but also the *constitution of a mule*. He always took care of his health, never keeping late hours but usually getting to bed by 9 P.M., rising early, and seeing a constant flow of patients in his office until 11 A.M., when he went to the German Hospital and

commenced his operations soon after noon, continuing until all the patients who had been scheduled had been operated on. This sometimes entailed as many as eighteen or twenty-four operations in one afternoon. It is true that he had his clinic so well organized that delays were almost unknown, and the facilities such that three or four operating tables might be in use at the same time. But it should be recorded that Deaver played a lone hand. He bore, "like the Turk, no brother near the throne." He did not use his assistant surgeons for what they were worth. He felt his obligation to the patient and to the family physician, and insisted on doing all the operations with his own hands; though, it is true, in later years, he usually allowed his resident physician to close the incision (practically all his operations were abdominal); and often, after making the incision himself, he would merely place the clamps (for a hysterectomy for instance), and then let the Resident complete the operation. In certain operations he excelled. He was an ardent advocate of Cæsarean section, which he was fond of referring to as "my operation"; and in difficult bile-duct operations I have never seen his superior either in this country or in Europe.

Doctor Deaver never took an active part in the administration of the societies to which he belonged. He declined to be nominated as president on the ground that he would be bored to extinction to have to sit through an entire session and listen to long and perhaps dull discussions on subjects better understood by himself than by the speaker, or about which he had no information and did not care to learn. So far as is known the only office he ever held in a Philadelphia society was that of a Vice-President of the Philadelphia Academy of Surgery (1918). In 1921-22 he was elected president of the American College of Surgery. As has been said elsewhere, he was a conspicuous figure in every medical gathering, especially distinguished by his wit, his dramatic method of expression, and his scientific experience. He has "brought down the house" many a time by his repartee. Who does not remember a recent meeting of this Association when he referred to one of his interlocutors as "Lordly Arthur"!

A Fellow of our Association since 1892, he brought to our meetings some of his most valuable work:

1893 Appendicitis.
1913 Pancreas.
1914 Pancreatitis.
1915 Gall-stones.
1916 Gastric and Duodenal Ulcer.
1917 Cholecystectomy; and Prostatectomy.
1920 Hysterectomy; and Goitre.
1921 Gastroenterostomy; and Pancreas.
1922 Peptic Ulcer.

A. P. C. A.

EDITORIAL ADDRESS

The office of the Editor of the Annals of Surgery is located at 131 St. James Place, Brooklyn, New York. All contributions for publication, Books for Review, and Exchanges should be sent to this address.

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227-231 South Sixth Street
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